ORIGINAL ARTICLE

Correlation of Fasting and Post Prandial Plasma Glucose with Hemoglobin Glycation

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ABSTRACT

Association of fasting plasma glucose (FPG) and post prandial plasma glucose (PPG) on hemoglobin glycation is still controversial. In this study we aimed to assess the influence of FPG and PPG on hemoglobin glycation in newly diagnosed never treated diabetic (NDNT-DM) subjects and treated diabetic (T-DM) subjects. One hundred and seventy seven diabetic subjects were included in this study. Plasma glucose concentrations were measured by hexokinase end point technique and glycated hemoglobin (HbA_{1c}) levels were measured by modified cation-exchange high performance liquid chromatography (HPLC). Univariate and multivariate linear regression models were applied to assess the relative contribution of FPG and PPG on HbA1c. Univariate linear regression analysis showed significant positive association of FPG and PPG with HbA1c in both groups. Multivariate regression model showed that ? (beta) value of HbA1c was 0.5528 ($p < 0.0001$) for FPG and 0.3047 ($p < 0.01$) for PPG in the NDNT-DM whereas 0.5509 ($p < 0.0001$) for FPG and 0.1874 ($p > 0.05$) for PPG in treated diabetic subjects. After adjustment for age and sex, beta remains statistically significant for FPG and PPG where beta value for FPG was higher for FPG than for PPG in both NDNT-TM group and T-DM groups. This study revealed that FPG has a stronger association on hemoglobin glycation as compared to PPG in diabetes mellitus.

Key words: Fasting plasma glucose, Post prandial plasma glucose, HbA_{1c}

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by rise in blood glucose level and derangement in protein and fat metabolism[1]. The formation of advanced glycation end products (AGEs) plays an important role for the development and progression of the long term complications of DM[2]. Glycated hemoglobin A (HbA1c) is the well characterized amadori product, produced in the early stage of AGE formation and the role of HbA1c in the management of DM is well established[3-5]. Measurement of HbA1c is an important component for the management of patients with diabetes mellitus, i.e., to monitor

long-term glycemic status, to judge the adequacy of diabetes management and to adjust therapies[6]. Epidemiologic studies and clinical trial established the association of HbA1c with the risk for long term complications of hyperglycemia[7-9]. The A1c Derived Average Glucose (ADAG) Study defined the mathematical relationship between HbA1c and average glucose (AG), similar to the mathematical relationship between HbA_{1c} and mean plasma glucose (MPG) in the Diabetes Control and Complication Trial (DCCT)[10,11]. The relationship between plasma glucose levels and HbA_{1c} is not consistent[12-15]. There are, however, insufficient data regarding the relative contribution of FPG and PPG in increasing the percentage of HbA_{1c}. It is very desirable and also meaningful to know whether FPG or PPG, alone or in combination plays the major role for hemoglobin glycation and thereby helpful in adjusting the therapy to achieve optimal HbA1c levels. In this study, multivariate linear regression model was applied to assess the relative strength of the association between plasma glucose and HbA1c in newly diagnosed never treated diabetic subjects and treated diabetic subjects.

Materials and Methods

One hundred and seventy seven specimens were collected from newly diagnosed never treated and treated confirmed diabetic subjects during January 2012 to June 2012. Fasting and post prandial blood specimens were collected for the estimation of fasting plasma glucose, post prandial plasma glucose (2 hrs after 75g oral glucose load and 2 hrs after breakfast) and estimation of HbA1c. Plasma glucose levels were measured by hexokinase end point techniques using Dimension RxL max automated analyzer (Siemens Healthcare Diagnostics Ltd.). HbA_{1c} were measured by modified high-pressure liquid chromatography (HPLC) method using D-10™ glycosylated hemoglobin testing system (Bio-Rad Laboratories, Inc., Hercules, CA, 94547, USA). Results are expressed as mean±SD. Univariate and multivariate linear regression models were applied to assess the relative strength of contribution of fasting or post prandial plasma glucose levels on hemoglobin glycation. Statistical analyses were performed by using STATISTICA version 8 for Windows.

Results

The mean±SD of age of the total study subjects was 48.4±12.3 years. Of the total 55.9% were males and 44.1% were females. Among them 57.06% were newly diagnosed never treated diabetic subjects and 42.94% were diabetic who used anti-hyperglycemic agents for the management of DM during the last three months. Characteristics of the study subjects are presented in table I.

Table I: Characteristics of the study subjects

Parameters	NDNT -DM (n=101)	T-DM (n=76)
Age (yrs)	46 ±12	52±11
Sex (M/F)	59/42	40/36
FBG (mmol/L)	8.9±3.3	8.8±4.1
PPG (mmol/L)	16.0±4.3	11.9±5.0
HbA 1c(%)	9.2±2.5	9.3±2.5

Univariate linear regression analyses showed that the ? (beta) value of HbA1c was 0.8067 ($p<0.0001$) for FPG and 0.7654 ($p<0.0001$) for PPG in the NDNT-DM group, 0.8105 ($p<0.0001$) for FPG and 0.7388 ($p<0.0001$) for PPG in the T-DM group. Multivariate linear regression analyses considering HbA1c as dependent variable and FPG and PPG as independent variables showed that the ? (beta) value of HbA1c was 0.5528 ($p<0.0001$) for FPG and 0.3047 ($p<0.01$) in the NDNT-DM and 0.5509 ($p<0.0001$) for FPG and 0.1874 ($p>0.05$) in the T-DM group. After adjustment for age and sex, beta remains statistically significant for FPG and PPG in both NDNT-TM group and T-DM group (Table II).

Table II. Influence of FPG and PPG on HbA glycation

Groups	Parameter	Beta () value	t-value	p value
NDNT-DM	FPG	0.5548	5.3065	<0.000
	PPG	0.3005	2.8672	<0.01
T-DM	FPG	0.5481	4.7219	<0.000
	PPG	0.2465	2.1489	<0.05

Discussion

In this study, we examined the relative contribution of fasting plasma glucose levels and post prandial plasma glucose levels on hemoglobin glycation in the newly diagnosed never treated diabetic subjects and treated diabetic subjects. Both univariate and multivariate linear regression analyses showed that the contribution of hemoglobin glycation is

higher for fasting plasma glucose levels than post prandial plasma glucose levels in both never treated and treated diabetic subjects. After adjustment for age and sex, the association between plasma glucose and HbA_{1c} remains statistically significant for FPG and PPG in both groups and contribution of fasting plasma glucose on hemoglobin glycation remains higher than the contribution of post prandial plasma glucose in both groups (Table II).

In this study, the relationship between fasting plasma glucose and HbA_{1c} is closer to DCCT[11] (~0.81 vs 0.82). The correlation coefficient between fasting plasma glucose and HbA_{1c} was higher than the correlation coefficient between post prandial plasma glucose and HbA_{1c} in control in the study population of Masram et al[13] (0.733 vs 0.699) whereas in type 2 diabetic subjects the relationship was found to be reversed (0.588 vs 0.776)[13]. Azim et al[14] also found modest relationship of FPG (r= 0.284) and PPG (r= 0.436) with HbA_{1c} and here PPG contributed higher in the glycation of hemoglobin. Another research group found that FPG levels showed better correlations with HbA_{1c} than with PPG levels in non-diabetic, pre-diabetic and newly diagnosed never treated diabetic subjects[12]. We observed similar trend of relationship between FPG and HbA_{1c}, PPG and HbA_{1c} in both never treated and treated diabetic subjects. Hossain et al[15] considered non-diabetic, newly diagnosed pre-diabetic and diabetic subjects and showed that FPG contributed higher than PPG in the glycation of hemoglobin. So the finding of this study is in concordance with the previous study done in Bangladeshi population[12,15] but inconsistent with the findings of studies done in abroad.[13,14] Therefore, measurement of fasting plasma glucose along with HbA1c may provide better outcome in the management of diabetic complications.

Conclusion

The contribution of fasting plasma glucose on hemoglobin glycation is higher than the contribution of post prandial plasma glucose levels in both newly diagnosed never treated and treated diabetic subjects.

References

1. Vinik A and Flemmer M. Diabetes and macrovascular disease. Journal of diabetes and its complications, 2002; 16: 235-45.
2. Gugliucci A. Glycation as the glucose link to diabetic complications. J Am Osteopath Assoc 2000; 100: 621-34.
3. Jeffcoate SL. Diabetes control and complications: the role of glycated haemoglobin, 25 years on. Diabet Med 2004; 21(7): 657-65.
4. Bunn HF, Gabbay KH, Gallop PM. The glycosylation of hemoglobin: relevance to diabetes mellitus. Science 1978; 200(4337): 21-7.
5. Kasezawa N, Kiyose H, Ito K, Iwatsuka T, Kawai H, Goto Y, et al. Criteria for screening diabetes mellitus using serum fructosamine level and fasting plasma glucose level. The Japanese Society of Multiphasic Health Testing and Services (JMHT), Fructosamine Working Committee. Methods Inf Med 1993; 32(3): 237-340.
6. Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2002; 48: 436-72.
7. Diabetes Control and Complications Trial Research Group. The effect of intensive diabetes treatment on the development and progression of long-term complications in insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. N Eng J Med 1993; 329: 978-86.
8. DCCT Research Group. The association between glyceamic exposure and long-term diabetic complications in the Diabetes Control and Complications Trial. Diabetes 1995; 44: 968-83.
9. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in type 2 diabetes (UKPDS 33). Lancet 1988;352:837-53.
10. ADAG Study Group. Translating the hemoglobin A1c assay into estimated average glucose values. Diabetes Care 2008; 31: 1473-8.
11. Rohlfing CL, Wiedmeyer HM, Little R, England JD, Tennill A, Goldstein DE. Defining the relationship between plasma glucose and HbA1c in the Diabetes Control and Complications Trial. Diabetes Care 2002; 25: 275-8.
12. Saiedullah M, Begum S, Shermin S, Rahman MR, Khan MAH. Relationship of glycosylated hemoglobin with fasting and postprandial plasma glucose in nondiabetic, pre-diabetic and newly diagnosed diabetic subjects. Bangladesh Medical Journal 2011; 40(1): 37-8.
13. Masram SW, Bimanpalli. Assessment of contribution of fasting and post meal plasma glucose to increased glycated hemoglobin in diabetes mellitus - A comparative study. Int J Biol Med Res 2012; 3(3): 2020-4.
14. Azim W, Gill MM, Azim S, Farooq W. Assessment of fasting and two-hour post-prandial glucose as an economical test for monitoring of glycemic control, compared to glycated hemoglobin. Medical Channel 2011; 17(2): 5-7.
15. Hossain T, Latif ZA, Sarkar AA. Relationship of HbA1c with fasting and plasma glucose 2 hours after oral glucose load in non diabetic and newly diagnosed pre diabetic and diabetic Patients. Birdem Med J 2012; 2(2): 81-3.