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SELF-MONITORED BLOOD GLUCOSE LEVEL TIMING TO REPRESENT HEMOGLOBIN A_{1C} LEVEL IN TYPE 2 DIABETIC PATIENTS

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ABSTRACT

Glycosylated hemoglobin A_{1C} (HbA_{1C}) is used to assess treatment efficacy in type 2 diabetic patients (T2DM). It is a function of both fasting and postprandial hyperglycemia. This study evaluated the relationship between different time point of self-monitored blood glucose (SMBG) testing and HbA_{1C}. Within 2 weeks, 64 T2DM patients at Police General Hospital, Bangkok, Thailand, performed 12-point SMBG (4 points per each meal per day on every other day: immediately pre meal, 1,2,and 4-hour post meal) twice . SMBG level was reported as mean level from two measurements. HbA_{1C} was measured 2 months later. SMBG levels of all 3 meals and of pre breakfast indicated good relationship with HbA_{1C} ($r = 0.766$, and $r = 0.689$, $p < 0.01$). SMBG level at 4-hour post lunch was also exhibited a good relationship with HbA_{1C} ($r = 0.671$, $p < 0.01$). Therefore, SMBG testing at 4-hour post lunch might be recommended as another good option to assess glycemic control in T2DM patients.

Keywords: Self-monitored blood glucose, Relation to, Hemoglobin A_{1C}, Type 2 diabetic patients

INTRODUCTION

In assessing glycemic control in type 2 diabetic (T2DM) patients, there are two ways to do it: self-monitoring of blood glucose (SMBG) and glycosylated hemoglobin A_{1C} (HbA_{1C}) measurement. [1, 2] HbA_{1C} is used to assess treatment efficacy. It is a function of both fasting and postprandial hyperglycemia.[3] HbA_{1C} testing should be performed routinely in all patients with diabetes, first to document the degree of glycemic control at initial assessment and then as part of continuing care. Measurement approximately every 3 months is required to determine whether a patient's metabolic control has been reached and maintained within the target range. [2] One disadvantage of HbA_{1C} testing is that it costs at least 4 times more than either fasting or SMBG blood glucose testing. On the other hand SMBG provides a real-time measurement of blood glucose. It helps in detecting hypoglycemia or post-prandial hyperglycemia.[2,4] Patients who use glucose meter at home exhibit significant improvement in fasting blood glucose level and HbA_{1C} after they started using the meter.[5] Since HbA_{1C} which is the best predictor of glycemic control in diabetic patients correlates well with mean daily blood glucose concentration. Many studies examined relationship between HbA_{1C} and blood glucose level in order to find a better understanding. Hoffman et al [6] found that mean blood glucose values for each of the pre meal SMBG testing were significantly correlated with HbA_{1C} in insulin treated T2DM patients. Peter et al [7] found that HbA_{1C} was strongly correlated with fasting plasma glucose (FPG) in newly diagnose treatment naïve T2DM patients. Sarwat et al [8] also found correlation between HbA_{1C} and individual SMBG measurement in T2DM treated with different type of insulin. In contrast Avignon et al [9] found that post-lunch (2 P.M) and extended post-lunch (5 P.M) plasma glucose was better correlated to HbA_{1C} than fasting values. Soonthornpun et al [10] demonstrated that postprandial hyperglycemia, specifically the 2-h postprandial glucose level, is associated with high HbA_{1C} level. Shimizu et al [11] suggested that postprandial breakfast and dinner were important in improving glycemic control in insulin treated patient

while Nakazaki et al [12] suggested that pre-and post-breakfast blood glucose levels are the most reliable predictors of 1- month later HbA_{1C} in type 2 diabetic outpatients who visit clinic every month.

There is still non-conclusive information about the best time point of self-monitored blood glucose level testing that can represent HbA_{1C}. Therefore, the aim of this study was to investigate the relationship between SMBG level obtained from different time point and HbA_{1C} in type 2 diabetic patients and to suggest the best time point in doing SMBG that can represent HbA_{1C} level.

MATERIALS AND METHODS

Study Design and Subjects

The prospective study was approved by the hospital ethic review boards and all patients gave written informed consent.

Type 2 diabetic patients who visited outpatient clinic of the Endocrinology Department of the Police General Hospital, Bangkok, Thailand were recruited into the study. Inclusion criteria were T2DM diagnosed for at least three months, had been treated with the stable dose of either oral antidiabetic agents and/or combined with insulin, had stable glycemic control define as having either HbA_{1C} level changed not more than 1% on 2 consecutive tests, if using any other medications they had to be stable at least 2 month before enrolled in the study, willing to do SMBG by themselves or allow caretakers to do. The exclusion criteria were patients who were pregnant or breast–feeding, had acute or chronic liver, pancreatic and renal diseases, had chronic infection, had co-existing diseases other than hypertension, dyslipidemia, and ischemic heart disease, had taken drugs that would affect glucose profile such as corticosteroids, had other endocrinopathies that affected glucose homeostasis.

Study Methodology

The patients who met the study criteria were recruited. Patient characteristics such as age, sex, duration of diabetes, co-existing diseases, current medication usage, height, weight were collected at the beginning of the study. Every patient or caretaker was trained and was instructed to performed 12-point SMBG (4 points per each meal per day on every other day) twice. Those 4 points were immediately pre meal, 1, 2, and 4-hour post meal. Accu-Check Advantage glucose meter (Roche Diagnostics, Thailand) was used. Patients were asked to follow their usual treatments and consumed their usual diets during the entire studied period. Patients recorded diet, the time they measured SMBG level, and the result of each blood glucose tested in the provided form. Telephone call to remind the patient about the testing schedule was made. Patients returned within two weeks with the results of their SMBG readings. HbA_{1C} level for each patient was measured 2 months after starting on the SMBG reading. HbA_{1C} was measured by high performance liquid chromatography assay (D-10 Hemoglobin Testing System, Bio-Rad™, Thailand).

Statistical Analysis

Patient characteristics data were analyzed by descriptive statistics. SMBG level of each time point was reported as mean level from two measurements. Pearson's correlation coefficients were calculated between HbA_{1C} and each of the SMBG value. Statistical significant was assumed when $p < 0.05$. Statistical analysis was performed using the SPSS program version 17.0.

RESULTS AND DISCUSSION

Characteristics of 64 T2DM patients who participated were shown in Table 1. They were elderly, overweight with longstanding diabetes and almost two-third of them used oral antidiabetic agents (60.9%). Most frequently used oral antidiabetic agent was metformin, followed by sulfonylureas. Combination of regular and intermediate acting insulin was most frequently used among 39.1% of patients who used insulin plus oral antidiabetic agents. Mean ± SD of SMBG level at each time point, Hemoglobin A_{1C} (HbA_{1C}) values and the correlation between SMBG level and HbA_{1C} were reported in Table 2, 3 , and 4 respectively. There was statistically significant correlation between every point of SMBG level and HbA_{1C} in all 64 type 2 diabetes and all were ranging from $r = 0.441$-0.766 ($p < 0.01$). The strongest correlation was between the mean total 3 meals (12 points) SMBG level and HbA_{1C} ($r = 0.766$, $p < 0.01$) followed by the pre breakfast level ($r = 0.689$, $p < 0.01$). Many studies had reported similar results about the correlation with the mean blood glucose (ranging from 0.70-0.92) and the pre breakfast blood glucose levels (ranging from 0.40-0.77) even though the degree of correlations reported were differed from our study. [3,9,13-22] This may be because blood glucoses in those studies mostly were drawn at two different time points usually pre breakfast or fasting and 2-hour post breakfast while in this study, mean blood glucose level derived from four measurements per meal per day (pre meal,1-,2- and 4-hour post meal) on every other day twice. In this study other point of SMBG that showed strong correlation with HbA_{1C} was

SMBG level drew at 4-hour post lunch (r =0.671, p < 0.01). This result was similar to the result suggested in one study that the postprandial glucose levels contributed more to the HbA_{1C} levels in patients with HbA_{1C} < 8.5% [23] and 52 of our patients had HbA_{1C} < 8.5%. In another study strong correlation was found at 5-hour post lunch (r=0.78). [9]

Our findings of blood glucose level timing that correlated with HbA_{1C} were different from these studies. One reason might be that the patients in this study were type 2 diabetic patients who were either using oral antidiabetic agents alone or using oral agents plus insulin. Due to the differences in the combination of medication used and the mechanism of action of the medication, the effect on blood glucose level might be difference. Therefore the glucose level timing that showed correlation might be different. In this study the correlation between SMBG level and HbA_{1C} at pre breakfast for all patients (n = 64; r = 0.689) was higher than in the subgroup of the patients taking only oral antidiabetic agents (n = 39; r = 0.652) and insulin plus oral agents (n = 25; r = 0.638). The correlation between pre breakfast SMBG level and HbA_{1C} in the oral antidiabtic agent user was greater than in the insulin plus oral agent had been reported in the study by Relimpio. [14]

This study has several limitations. First, the study was done by the patients under real-life situation. The food intake, patients' behaviors such as medication non-adherence had not been strictly controlled and may have some effects on the blood glucose levels. Second, the timing of SMBG level performed. The patients performed 12-point SMBG level (4 points per each meal per day on every other day) twice in 2 weeks. This could be a confounding factor since it was not done on the same day. This could lead to an under- or overestimation of blood glucose values especially when the food intake was much different. Third, majority of our patients had HbA_{1C} < 8.5%, extrapolation to patients with higher HbA_{1C} level should be done with caution. Fourth, the patients included in this study were stable type 2 diabetic patients, without any liver/kidney diseases or any diabetic related complications other than hypertension, ischemic heart disease or dyslipidemia. Therefore, the results may not be extrapolated to all diabetic patients.

CONCLUSIONS

There were correlations between every point of SMBG level performed and HbA_{1C} in all 64 type 2 diabetic patients and all were statistically significant ranging from r = 0.441-0.766. The mean SMBG levels obtained from 3 meals (average 12 points) correlated best with $HbA_{1C;}$ however it was difficult to do all 12 points in the real-life situation. SMBG levels at pre breakfast or at 4- hour post lunch also correlated well with HbA_{1C}. Therefore, apart from pre breakfast blood glucose level that was routinely measured, a 4- hour post lunch glucose level might be another good option to do the measurement.

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Table 1. Characteristics of the patients

Characteristics	
n	64
Age(years)	60.0 ± 10.1
Sex (female)	57.8%
BMI($kg/m^{2)}$	26.2 ± 3.7
≥ 23.0 kg/m^2	81.3%
Duration of diabetes (year)	11.2 ±7.1
Co-existing diseases¶	
HTN	10.9 %
DLP	20.3 %
HTN+ DLP	60.9 %
Medication	
Oral agent	60.9 %
Insulin plus oral agent	39.1 %

Data were mean ± SD, unless otherwise indicated. ¶ Total less than 100 % because some patients had other combination of co-existing diseases HTN = Hypertension, DLP = Dyslipidemia

Table 2. Self-monitored blood glucose (SMBG) level (mmol/L)

SMBG level	Mean ± SD
Pre Breakfast	7.41 ± 1.99
1-h post Breakfast	10.63 ± 2.86
2-h post Breakfast	8.84 ± 2.59
4-h post Breakfast	7.13 ± 2.54
Breakfast (total 4 points)	8.49 ± 1.98
Pre Lunch	7.52 ± 2.44
1-h post Lunch	8.91 ± 2.30
2-h post Lunch	8.75 ± 2.52
4-h post Lunch	8.01 ± 2.71
Lunch (total 4 points)	8.31 ± 2.07
Pre Dinner	7.79 ± 2.14
1-h post Dinner	9.54 ± 2.42
2-h post Dinner	9.03 ± 2.55
4-h post Dinner	7.62 ± 2.22
Dinner (total 4 points)	8.48 ± 1.77
Total (3 meals;12 points)	8.42 ± 1.77

Table 3. Hemoglobin A_{1C} (HbA_{1C}) values

HbA_{1C} (%)	Frequency	Percent
5.1-6.0	8	12.5
6.1-7.0	19	29.7
7.1-8.0	20	31.3
8.1-9.0	13	20.3
9.0-10.0	1	1.6
>10.1	3	4.7

Table 4. Correlations between SMBG and hemoglobin A_{1C} (HbA_{1C}) levels

SMBG level	Pearson correlation (n=64)
Total (3 meals;12 points)	.766**
Breakfast	.700**
Lunch	.713**
Dinner	.619**
Pre breakfast	.689**
1 h post breakfast	.441**
2 h post breakfast	.601**
4 h post breakfast	.535**
Pre lunch	.631**
1 h post lunch	.479**
2 h post lunch	.583**
4 h post lunch	.671**
Pre dinner	.504**
1 h post dinner	.517**
2 h post dinner	.535**
4 h post dinner	.524**

** Correlation is significant at the 0.01 level (2-tailed)

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