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ARTICLE

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Evaluation of Clinical Effectiveness of Self-Monitoring Blood Glucose Level in Patients with Type 2 Diabetes Mellitus Treated with Non-Insulin Regimens in Düzce: Primary Care-Based Study

ABSTRACT

Objective: Self-monitoring blood glucose (SMBG) is frequently recommended, beside its controversial efficacy. Herein, it was aimed to evaluate frequency of SMBG and its efficacy among patients with type 2 diabetes (T2DM) in primary care settings in Düzce Province of Turkey.

Methods: The cross-sectional and primary care-based study enrolled a total of 680 patients with T2DM treated with oral anti-diabetic agents. Status of SMBG was recorded as non-use, daily, weekly and monthly. Metabolic and glycemic indexes were compared according to statuses of SMBG use.

Results: Over the two-third of the patients were user of SMBG. The frequency of daily, weekly and monthly use of SMBG was 13.2%, 32.1% and 24.5%, respectively. Of them, the majority have irregularly used SMBG (59.4%). However, the ratio of patients who have regularly used SMBG was just 24.3%. No significant difference was observed between statuses of SMBG in glycemic indexes of HbA1c, Fasting blood glucose and post-prandial blood glucose (p=0.655, p=0.721 and p=0.389).

Conclusions: Although the high and irregular use of SMBG, there was no difference between status of SMBG. Therefore, the family physicians should consciously advice self-monitoring blood glucose. It should be recommended after the patients are competent and empowered with education for its use. Further investigations should be carried out to general idea on clinical effectiveness SMBG in Turkey.

Keywords: Type 2 Diabetes Mellitus, Primary Care, Self-Monitoring Blood Glucose, Glycemic Control

Düzce İlinde İnsülin Kullanmayan Tip 2 Diyabet Hastalarında Kendi Kendine Kan Şekeri İzleminin Klinik Etkinliğinin Değerlendirilmesi: Birinci Basamak Tabanlı Bir Çalışma

ÖZET

Amaç: Kendi kendine kan şekeri (SMBG) takibi sıklıkla tavsiye edilmesinin yanında, etkinliği tartışmalıdır. Burada, SMBG kullanımının diyabetteki sıklığını ve Türkiye’de Düzce ilinde birinci basamakta tip 2 diyabet (T2DM) olan hastalarda etkinliğinin değerlendirilmesi amaçlanmıştır.

Yöntem: Kesitsel ve birinci basamak-tabanlı çalışmaya oral anti-diyabetik ajanlar ile tedavi olan T2DM’li toplam 680 hasta alınmıştır. SMBG kullanım durumu kullanmayan, günlük, haftalık ve aylık kullanan seklinde kaydedilmiştir. Metabolik ve glisemik indeksler SMBG kullanım durumuna göre karşılaştırılmıştır.

Bulgular: Hastaların 2/3 ten fazlası SMBG uygulamaktadır. Günlük, haftalık ve aylık SMBG kullananların oranı sırası ile 13,2%, 32,1% ve 24,5% idi. Bunların da çoğunluğu düzensiz kullanıyordu (59,4%). Fakat düzenle kullananların oranı 24,3%. SMBG kullanım durum grupları arasında HbA1c, Açlık kan şekeri ve tokluk kan şekeri olan glisemik indeksler için farklılık gözlenmemiştir (Sırası ile p=0.655, p=0.721 ve p=0.389).

Sonuç: Yüksek ve düzensiz SMBG kullanımı olsa da, SMBG kullanım durumları arasında hiçbir fark yoktu. Bu nedenle, aile hekimleri kendi kendine kan şekeri izlemini dikkatli ve bilinçli olarak tavsiye etmelidir. Hastalar eğitimle bilgilendirilmiş ve kendi yeterliliklerini kazanmasından sonra SMBG kullanımı önerilmelidir. Türkiye’de SMBG kullanımının klinik etkinliği hakkında genel bir kantar için ileri düzeyde araştırmalar yapılmalıdır

Anahtar Kelimeler: Tip 2 Diyabetes Mellitus, Birinci Basamak, Kendi Kendine Kan Şekeri İzlemi, Glisemik Kontrol

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic alterations characterized by hyperglycemia resulting from defects in insulin secretion and action or both. The patients present with a combination of varying degrees of insulin resistance and relative insulin deficiency, and it is likely that both contribute to type 2 diabetes mellitus (T2DM). It has already been established that chronic hyperglycemia of DM is associated with long-term complication and dysfunction (1-3). The prevalence, incidence, mortality, morbidity, cost to society, and the effectiveness of treatment and prevention are discussed. Primary preventable measures involving weight management and exercise are aimed to establish glycemic and metabolic control, eventually preventing micro and macrovascular complications in diabetic patients (4, 5). Early interventions can reduce complications specific to DM, such as end-stage renal disease, blindness, and lower extremity amputations (6-8). One of the most important stages of management in diabetes mellitus is monitoring of blood glucose measured with a glucometer. Self-monitoring of blood glucose (SMBG) is a recognized diabetes monitoring method (9). It is recommended for patients in order to achieve the desired glucose levels, prevent hypo- and hyperglycemic incidents, and thus to prevent acute and chronic diabetic complications (10-12). This method is recommended mainly for patients with T1DM, and particularly for those with T2DM treated with insulin regimens and on alternative treatment (13).

There are some suggestions that SMBG improves long-term prognosis of diabetes. However, no evidence of beneficial effect of SMBG in near normo-glycemic patients has been provided (14, 15). A recent study of meta-analysis including twenty-two randomized controlled trials reported that an overall significant effect on glycemic control, patient satisfaction and general well-being among patients who used SMBG at 12 month follow-up. A review suggested that SMBG is of limited clinical effectiveness in improving glycemic control in patients with T2DM on oral agents, or diet alone, and is therefore unlikely to be cost-effective (16,17).

Its efficiency depends on additional instructions in incorporating the results into self-care. It emphasizes the importance of adequate education which motivates the patient and allows SMBG to be effective. Another debate is cost-effectiveness of SMBG in T2DM (18). Nevertheless, SMBG is routinely recommended for patients who are not using insulin. Decisions about the prescribing strips for blood glucose test and advising blood glucose monitoring require consideration of information about the costs and clinical benefits (19-21).

To best our knowledge, there was no any study in which clinical effectiveness of blood glucose monitoring at home was investigated in primary care settings in Turkey, but one study, conducted by Baltacı et al., compared the effectiveness of SMBG between statuses of SMBG use among T2DM encountered at tertiary hospital. In the current study, it was aimed to investigate the frequency and efficacy of SMBG use on glycemic control among T2DM patients managed with non-insulin regimens in the current study, based on the light of this report.

MATERIALS AND METHODS

Study design and patient enrollment

The study was designed as cross-sectional and primary care-based study implemented in Duzce in 2011. The study enrolled 680 type 2 diabetic patients managed with non-insulin regimens, who were referred to diabetes clinic of Duzce University Hospital from primary care settings. A semi-structured study survey, developed in previous study, was applied to participants by one of the physician investigators in face to face interview and physical examination was done on admission. The survey include the age, duration of DM, weight, height, gender, education, smoking habit, residency, presence of co-morbid diseases, status of complication (previously and currently detected on admission), presence of hypoglycemia (self-reported) and SMBG frequency were recorded. Lipid profile, fasting and post-prandial blood glucose, HbA1c, spot urinary creatinine and microalbumine excretion were assayed on admission. Inclusion criteria were T2DM, oral informed consent and co-operation to understand the study survey. Status of complications such as nephropathy, retinopathy, coronary artery disease, neuropathy, diabetic foot, and cerebrovascular events were collected from medical records and medical history of the patients enrolled in the study. Exclusion criteria were cancer, T1DM, T2DM managed with insulin regimen and non-cooperation to understand the study survey. For illiterate subjects, the study survey was read and filled by researchers.

Sample collection

In the study, blood sample was collected from venous circulation in the morning times and overnight fasting. In all patients, HbA1c (%) was measured from whole blood samples of patients made with Cobas C501 brand (Roche Hitachi Diagnostic Systems) biochemistry auto-analyzer device. Fasting blood glucose (FBG V), post-prandial blood glucose (PBG mg/dL), Light density (LDL-chol mg/dL) and high density lipoprotein cholesterol (HDL-chol mg/dL), triglyceride (TG mg/dL) and total cholesterol (total-chol mg/dL) were measured. Spot urine sample was collected in

the morning voiding. Body mass index was calculated with formula of [weight (kg) divided by height square (m^2)]. Albumin-creatinine ratio (ACR) was calculated as urinary albumin \times 1000/urinary creatinine and stated as mg/day. In case of ongoing menstruation and suspected urinary infection, urinary sample collection was postponed. Albuminuria was defined as positive if spot urinary ACR was over 30 gr/day.

Ethics

The ethics of study was approved by Ethic committee of Duzce University Medical Faculty and was consistent with has been performed in accordance with the ethical standards laid down in the Declaration of Helsinki (1964 and 2013), and the permission for the study implementation in primary care health centers throughout Turkey was obtained from Department of Family Medicine, Health Ministry of Turkey. All participants were informed about the study by cover sheet that is attached to study survey and informed consent was obtained. The study survey was anonymous, did not contain any critical questions, and confidentiality of the data were maintained.

Data Analysis

SMBG frequency was assessed with daily (once a day, twice a day, and three or more times a day), weekly (once a week, two times a week, and three or more times a week) and monthly (once a month, and two times a month). Also, the patients who have never implemented SMBG at home were recorded. The subjects were assigned into four subgroups according to status of SMBG use as I: those who implemented daily SMBG, II: weekly SMBG, III: monthly and IV: non-user of SMBG. Also, the subjects were allocated into three subgroups according to status of SMBG defined by ADA criteria as group 1: T2DM subjects who have regularly used SMBG, group 2: those who have irregularly, and group 3: those who have never used SMBG (23). Glycemic control was assessed with serum level of HbA1c, fasting and post-prandial glucose. Metabolic control was assessed with lipid profile. Glycemic and metabolic control indexes were compared with subgroup of SMBG frequency as daily, weekly and monthly use. SMBG frequency was allocated to three groups as regular, irregular and non-SMBG use according ADA criteria. Education level and gender distribution diabetic complication, lipid profile, HbA1c, age, Duration of DM and hypoglycemia were stated and compared between groups of regular, irregular and never use of SMBG.

Statistical Analysis

For statistical analysis, SPSS version 15.0 (IL) was used. Descriptive values of categorical variables and numerical variables were stated as frequency and percentage and mean \pm SD respectively. We used chi – square (X^2) test for

relation between categorical variables. Normal distribution of variables was assessed using Kolmogorov-Smirnov test. Logarithmic transformation was applied for continues variables which were not normally distributed (fasting blood glucose, post-prandial blood glucose, HbA1c, LDL-chol, HDL-chol, Total-chol, TG and spot urinary albumin-creatinine ratio (ACR). Firstly, simple ANOVA was used for logarithmically transformed variables between groups of SMBG status Unadjusted mean and standard deviations were computed after simple ANOVA. Statistical significant was set, if p value was less than 0.05.

RESULTS

A total of 680 patients with T2DM were enrolled. The mean age was 55.4 ± 10.8 (32-85 years-old). Of them, they were 403 (59.2%) females aged 33-73 years and 277 (40.8%) male aged 30-85 years. Among the patients, ratio of current smokers was 18.8 %. The majority of the patients (49.6 %) were graduated from primary-secondary school. Duration of diabetes mellitus was 6.9 ± 4.3 (1 to 36 years). Mean BMI was 32.7 ± 5.9 (23.6-60.4 kg/m^2).

The 83.8% of the patients ($n = 570$) stated that they have used a glucometer for SMBG at home. The ratios of daily, weekly and monthly use of SMBG us were 11.4 % ($n = 77$), 43.9 % ($n = 299$), and 28.3 % ($n = 192$), respectively. Of the patients, 16.3 % have never implemented SMBG. Among the SMBG users, ratio of patients who have regularly used SMBG was 24.4 %. The majority have irregularly used SMBG (59.4 %). Between male and female subjects, no significant difference was observed in distribution of SMBG frequency ($p = 0.418$) (Figure 1).

Effectiveness of SMBG frequency use of daily (I), weekly (II), monthly (III) and non-user (IV) was compared with glycemic indexes (HbA1c, FBG and PBG) and metabolic indexes (LDL-chol, HDL-chol and TG). Mean HbA1c values were 7.4%, 7.4%, 7.8% and 7.7% for group I, II, III and IV, respectively. Mean levels of FBG and PBG among groups of SMBG frequency use were given in figure 2. Mean HbA1c, FBG and PBG values of glycemic indexes were not significantly different between groups of SMBG frequency use ($p = 0.655$, $p = 0.721$ and $p = 0.389$) (Figure 2).

Education level and gender distribution diabetic complication, lipid profile, HbA1c, age, duration of DM and hypoglycemia were stated and compared between groups of regular, irregular and never use of SMBG. The patients with higher education level were likely to regularly use SMBG, compared to those with low education level ($p = 0.026$). Male patients versus female patients seemed to use regularly SMBG, but there was no significant differences in status of SMBG implementation between male and female patients ($p = 0.112$).

Duration of DM was observed longer in group 1 and 2, compared to group 3 ($p = 0.005$, $p = 0.012$). HbA1c levels between groups of SMBG status were not significantly different ($p = 0.083$). HDL-Chol, LDL-Chol and TG levels were not significantly different between groups ($p = 0.148$, $p = 0.127$ and $p = 0.079$, respectively). Totally, hypoglycemic events were observed in 15.7 % of the patients. When the number of patients with degree of hypoglycemia between groups was compared, the frequency of patients with high number of hypoglycemic events was detected in group 2 (47.2 %), but not statistically significant (p

$= 0.081$). One of the any diabetic complications and of the co-morbid diseases was observed in 47.1 % and 64.7 % of subjects, respectively. When presence of diabetic complication and co-morbid disease was compared with status of SMBG frequency, no significant difference was observed between groups of SMBG frequency ($p = 0.607$ and $p = 0.247$, respectively). We found that the patients with albuminuria were statistically higher in group of irregular SMBG use (23.2 %) than group of regular (11.9 %) and never user SMBG (13.3 %), ($p = 0.005$) (Table 1).

Table 1. Comparison of SMBG status with basic socio-demographic and clinical features

Variables	SMBG Status (%; mean \pm SD)			p
	Regular Use	Irregular Use	Never Use	
Education level				0.026
Illiterate	8.9	15.3	21.3	
Literate, but informal	13.8	13.8	16.1	
Primary-secondary school	51.6	51.5	52.2	
High school	15.4	12.3	6.3	
University and upper grade	10.3	7.1	4.1	
Gender				0.112
Male	41.9	37.7	35.1	
Female	58.1	62.3	64.9	
Complication (+)	44.1	52.9	37.4	0.083
Age (years)	55.8 \pm 10.4	56.6 \pm 10.4	56.01 \pm 11.8	0.315
LDL-Chol (mg/dL)	123.2 \pm 41.5	126.9 \pm 39.3	123.9 \pm 32.6	0.127
HDL-Chol (mg/dL)	48.7 \pm 16.2	46.6 \pm 12.1	47.2 \pm 13.8	0.148
TG-Chol (mg/dL)	179.6 \pm 119.7	174.3 \pm 87.4	178.6 \pm 88.4	0.079
Duration of DM (years)	7.2 \pm 5.4	6.9 \pm 5.8	6.6 \pm 5.7	0.023*
HbA1c (%)	7.4 \pm 1.9	7.6 \pm 1.6	7.5 \pm 1.7	0.083
Albuminuria (+)	11.2	23.2	13.3	0.005**
Hypoglycemia (+) (n = 113)	29.7	47.2	23.1	0.081
Mild	55.6	58.2	57.1	
Moderate	29.6	27.9	19.1	
Severe	14.8	13.9	14.3	
Co-morbid disease (+)	66.9	74.3	64.9	0.181

*ANOVA test was used and duration of diabetes mellitus among patients in group was higher than that of those irregular and never use of SMBG (0.005; 0.012; 0.086). ** Chi-square test was used. SD: Standard deviation

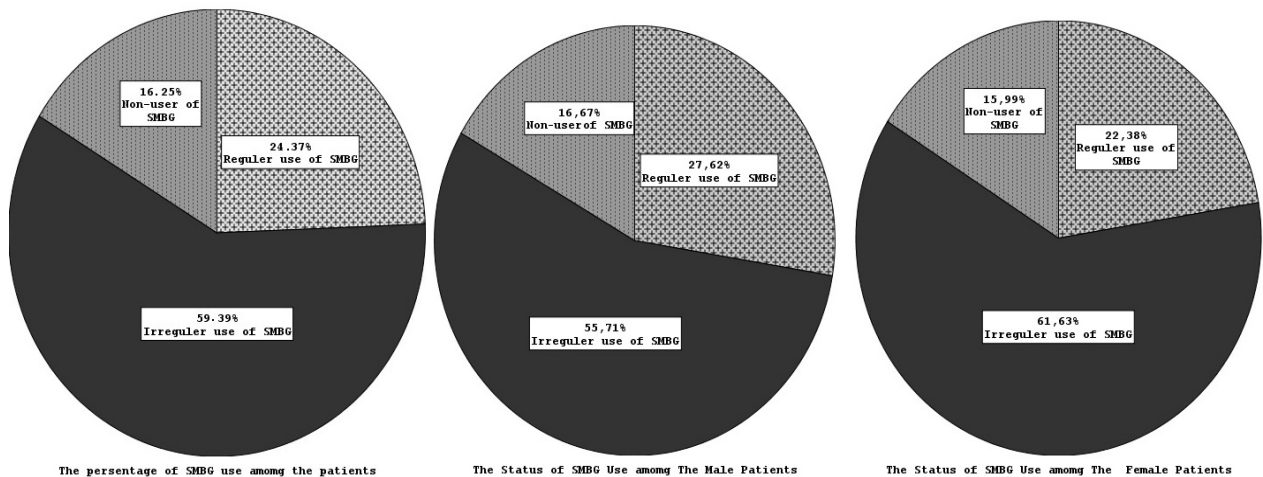


Figure 1. Distribution of use of SMBG frequency

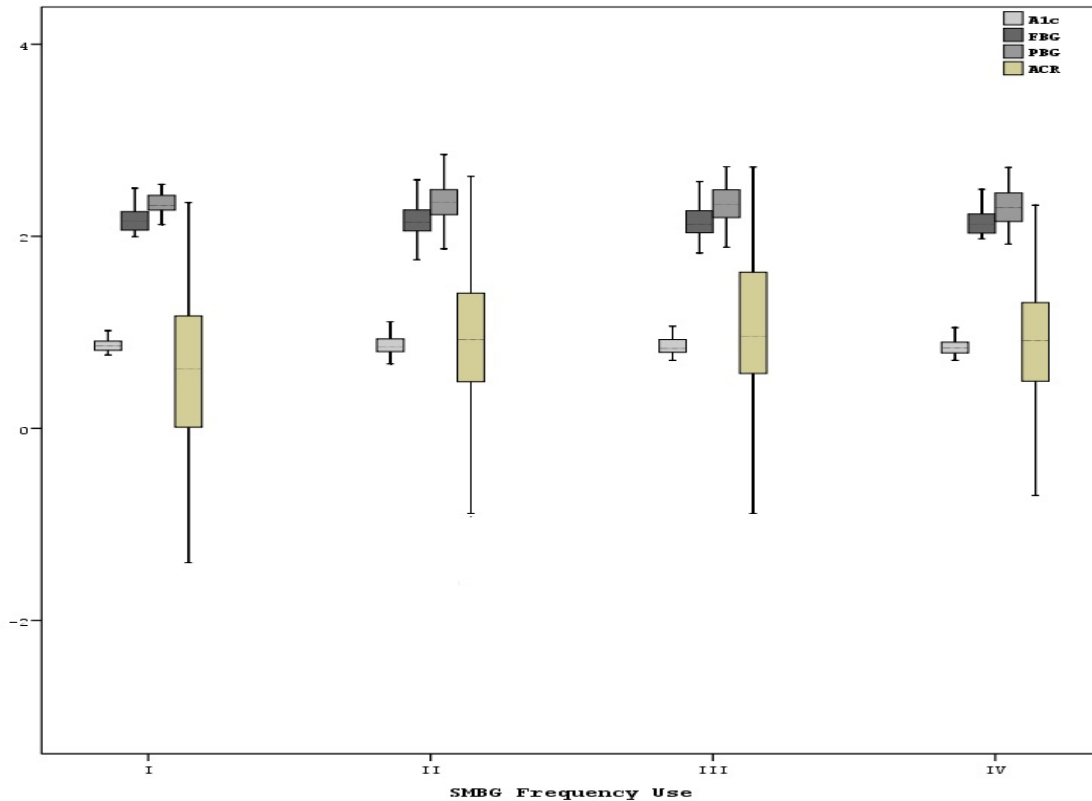


Figure 2. Comparison of HbA1c, FBG, PBG and ACR between daily, weekly, monthly and never use of SMBG frequency

DISCUSSION

The study indicated that ratio of SMBG users (both regular and irregular) among patients with T2DM managed with oral anti-diabetic drugs was considerably high, and the majority of them have irregularly implemented SMBG. Our study also showed that SMBG implementation had no significant benefits and effectiveness on glycemic control and there was no correlation between SMBG frequency and glycemic control indexes.

The usefulness of SMBG has been demonstrated in T1DM by improvement in glycemic control, and long-term prognosis in patients, by extension, in patients with T2DM managed with insulin regimens. SMBG has been recommended in T2DM for special situations such as insulin therapy administration and presence of frequently experienced hypoglycemia (24,25).

Fremantle Diabetes Study by Davis et al. showed that self-reported hypoglycemia was significantly higher in any SMBG group than non-SMBG group (33.5 % versus 21.3 %) (26). In Contrast, we did not find any significant difference for self-reported hypoglycemia between SMBG groups. In case of complication development or for prevention of complications in patients with uncontrolled blood glucose, SMBG implementation has been recommended to obtain desired blood glucose (23). In the study, there was no significant difference in the presence of complication recorded

between groups of SMBG status. In some studies, it was claimed that SMBG efficacy on metabolic control in patients with T2DM was dependent on some defined conditions. Schwedes et al. suggested that meal-related structured SMBG could improve glycemic control in T2DM treated with non-insulin regimen (27). Franciosi et al. reported that SMBG could be an important role in metabolic control if it is an integral part of a wider educational strategy devoted the promotion of patient autonomy (28).

Our study revealed that the percentage of the patients who have regularly used was comparably higher among patients with upper education level. Other defined conditions such as patient's expectation and perspective on SMBG were not investigated in the current study. Patient's expectation, knowledge level and satisfaction may have effects on SMBG preference and SMBG awareness as well as patient's education level.

Effectiveness of SMBG on glycemic control remains controversial in T2DM treated with diet and oral anti-diabetic agents. DiGEM trial by Simon and colleagues revealed that SMBG was associated with higher cost and lower quality of patients with non-insulin treated T2DM, as well as no clinical significant outcome (29). ASIA study by Guerci et al. reported that significant improvement in glycemic control by lowering HbA1c in SMBG group, compared to conventional group (30). The

current study found that SMBG had no significant efficacy on glycemic and metabolic control in the patients, when metabolic and glycemic control index such as HbA1c, lipid profile and blood glucose level were compared in both groups of SMBG status and frequency. Moreover, the current study revealed no significant association between SMBG delivery and complication development.

Duration of DM and age are among main factors for development of diabetic complications. With increased duration of DM and age, there is great risk for complications as well as glycemic control (31). We found that duration of T2DM and age had effect on glycemic control in our study after we used covariant analysis. In the current study, duration of T2DM was not significantly different between groups. Mean age was also similar between groups of SMBG status. That was why the frequency of complications between groups was not significantly different in the present study; therefore, we suggest that SMBG has no significant effect on prevention of diabetic complications.

Hypoglycemia is frequently experienced by the patients with T1DM and T2DM treated with insulin regimens and sometimes with sulfonylurea groups of oral anti-diabetic agents. SMBG helps protect patients by allowing them to immediately confirm acute hypoglycemia (32-34). Clinical trials are not designed to achieve an outcome of hypoglycemia, primarily due to patient safety and ethical concerns. Therefore, clinical studies of SMBG are lacking with respect to the relationship between hypoglycemia and SMBG. Hypoglycemia can force patients to frequently monitor blood sugar at home. We observed that severe hypoglycemia attacks reported by the patients were more frequent in group 1 and 2, but not significant, than group 3. That might be why the frequency of the patients who had regularly and irregularly used SMBG were observed as higher.

The price for the strips of glucometer was reimbursed to patients in our country. It seems to be motivating the patients with T2DM for SMBG use. However, it might be one of the reasons leading the patients to use haphazardly. In the study, cost-effectiveness was not studied. This is another issue which should be discussed. Further studies on cost-effectiveness of SMBG use among patients T2DM who consciously or haphazardly use SMBG were needed. One of the largest follow-up studies, Fremantle study did not support a relationship between SMBG and improved survival in a well-characterized population-based study of patients

with T2DM, but ROSSO investigators that SMBG was associated with decreased diabetes-related morbidity and all-cause mortality in type 2 diabetes (35, 22). Our result was consistent with former but not with latter study. These different results can be due to socio-demographic features of patients.

One of the study limitations was that the study was designed as cross-sectional. Glycemic index parameters were assessed once on admission during the study. It would be better that prospective and controlled study can indicate whether SMBG is effective or not. Fluctuations of blood sugars and HbA1c levels were not evaluated in the current study. There was more than one factor which could affect glycemic index parameters. In the study, we applied co-variant analysis. In this way, potential factors on index parameters of glycemic control were tried to be clarified. We did not include methods and time of SMBG delivery and application. This was another limitation that time of SMBG use would have provided us information about when patients have used it, before or after the meal. Third limitation of the study was that treatment modalities were not compared between groups of SMBG status and SMBG frequency. Lastly, presence of hypoglycemia and complications, not at all, were obtained with self-report of the patients.

CONCLUSION

We consider that self-monitoring blood glucose is important, but it haphazardly has been used among the patients with T2DM. We suggested that the patients should not use SMBG unconsciously, and the physicians should set unique intervention for the diabetic patients and encourage them to advice other interventions for glycemic control. The physicians, especially family physicians, can advise SMBG implementation to their patients for various reasons, but they should recommend SMBG after educating the patients and providing patient's empowerment and adhesion. In family practice, promoting patient empowerment provide more patient adhesion and consistency for disease management. Further investigations regarding comparisons between treatment modalities and SMBG frequencies as well as patient's satisfaction, expectation and empowerment on SMBG use in T2DM are needed.

Statement of Conflicts of Interest

The authors state no conflict of interest

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