

# Investigation of Blood Glucose Profile by Continuous Glucose Monitoring (CGM)

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## Abstract

**Background:** Diabetes has been great problem worldwide. Continuous Glucose Monitoring (CGM) has been in focus, and useful CGM, FreeStyle Libre (Abbott) has been introduced to clinical ordinary practice of medicine.

**Case and results:** The patient was 57 year-old female with type 1 diabetes mellitus (T1DM), who showed BMI 20.6 kg/m<sup>2</sup>, HbA1c 8.6%. She was on CGM measured glucose every 15 minutes in 24 hours for 14 days. Treatment included 3 times of Insulin Aspart and once of Insulin Glargin. She showed characteristic pattern of blood glucose profile according to the working schedule of the day.

**Discussion and conclusion:** The beneficial points of FreeStyle Libre have been convenient and accurate for clinical use for reducing hypoglycemia episodes. Treatment using CGM associated with multiple daily insulin injection (MDI) confers similar or greater benefits for glycemic profile. When evening insulin was not injected one day, blood glucose increased 320 mg/dL, suggesting 64 g of carbohydrate ingested for supposed calculation. These results suggest that CGM could recommend the timing and doses of insulin injection according to the lifestyle of the patients with clinical merit.

**Keywords:** Continuous glucose monitoring; FreeStyle libre; Type 1 diabetes mellitus; Type 2 diabetes mellitus; Blood glucose profile

**List of abbreviations:** DCCT: Diabetes Control and Complications Trial; ADA: The American Diabetes Association; MDI: Multiple Daily Insulin; rtCGM: real-time Continuous Glucose Monitoring; FDA: Food and Drug Administration

## Introduction

The prevalence of diabetes has been increasing globally and a multifactorial approach is necessary to decrease several risk of complications in this situation [1]. Maintaining the adequate blood glucose has been the key to prevent microvascular and macrovascular diseases [2]. Consequently, optimizing glucose levels has been required for the patients with Type 1 Diabetes Mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) [3].

There have been treatment of insulin therapy for older adults with T1DM and T2DM, and it has performed successfully with the development of continuous glucose monitoring (CGM).

Patients with T1DM have been living longer [4], and its number of older adults has been growing [5]. Consequently, insulin-treated older T1DM patients have longer diabetic history and tend to have micro- and macrovascular complications and other comorbidities [5,6].

Such patients have higher risk for severe hypoglycemia, leading to other severe states such as cerebral vascular accident (CVA), myocardial infarcts, arrhythmias, temporary or permanent cognitive impairment and death [5,7].

In order to avoid hypoglycemia, The American Diabetes Association (ADA) has recommended higher HbA1c and glycemic goals which vary according to each comorbid status in older adults [6]. CGM has been effective for avoid

hypoglycemia and the The DIAMOND study with T1DM treated with multiple injection therapy, showed improved HbA1c with less hypoglycemia [8]. This study was a prospective, randomized clinical trial of CGM for adults.

There has been a useful device for CGM, which has been introduced to clinical practice. It is FreeStyle Libre, produced by Abbott, USA [9,10]. In this study, daily profile of blood glucose in patient with T1DM was measured by FreeStyle Libre and investigated detail glucose fluctuation.

## Case Presentation

The patient was 57 year-old female with T1DM. She was diagnosed as T1DM 10 years ago, and has been continued insulin therapy after that. Her recent HbA1c has been around 7.5%-8.6% and blood glucose ranges from 50 mg/dL to 400 mg/dL. These results are supposed to be rather unstable and not in satisfactory diabetic controlled state.

Consequently, we tried to evaluate her current diabetic condition in detail, and we have measured the profile of blood glucose using FreeStyle Libre (Abbott).

On physical examination, her consciousness and vitals are normal, and heart, lung, abdomen and neurological findings were unremarkable. She showed 159 cm in height, 52 kg in weight, BMI 20.6 kg/m<sup>2</sup>, abdominal circumference 83 cm and thigh circumference 42 cm.

Laboratory findings on January 2018 were as follows: postprandial blood glucose on 216 mg/dL after 150 min of meal, and HbA1c was 8.5%. She showed unremarkable data about complete blood count, liver function test, renal function and lipids profile.

Current insulin treatment included Novo rapid (Novo Nordisk) 3 times a day, and Insulin Glargine (Eli Lilly and Company) of once a day. The former is Insulin Aspart given by pre-filled pen including 100 units/mL, and the latter is Insulin Glargine by BS injection kit FFP including 300 units/mL. The time and units are as follows: the former is injected 8, 10, 10 units on 0700h, 1230h, 1830h and the latter is injected 11 units on 2300h.

## Continuous glucose monitoring

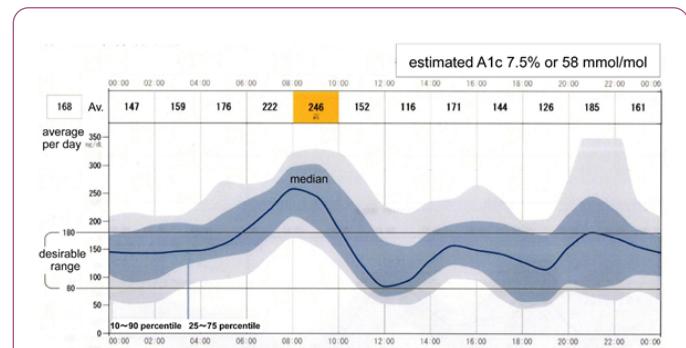
CGM was studied for 14 days. Using CGM device, blood profile were measured every 15 minutes in 24 hours. We used sensor-based device for blood glucose monitoring, which is the FreeStyle Libre Flash Glucose Monitoring system, produced by Abbott Diabetes Care Inc, Alameda, CA, USA. This is firstly commercial-based available sensor systems associated with several beneficial points [11,12].

It has some advantages for replacing blood glucose testing and detecting trends and tracking patterns in order to detect the episodes of hyperglycemia and hypoglycemia. Characteristic strong points are accurate, convenient and small size for practical use [10,13]. The sensor is put and wearable on the back of the upper arm during 14 days and can

automatically preserve swinging glucose data every 15 min for 14 days [9,10,14,15].

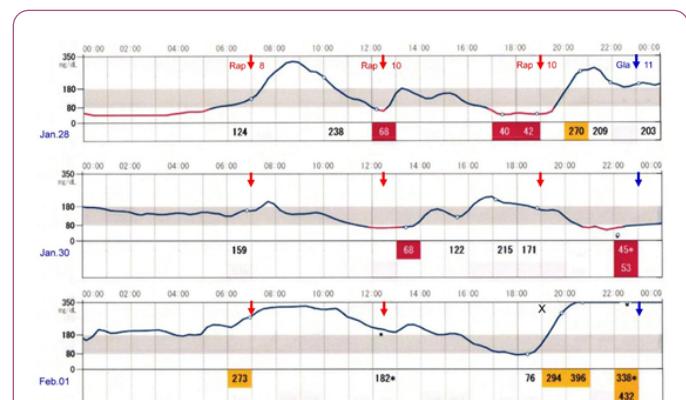
## Results of CGM

The mean value of the glycemic profile over 14 days is shown in **Figure 1**. In general, blood glucose tends to rise at 0800-1000 h after breakfast intake. During working, she keeps on walking all the time, then blood glucose level usually falls around 1100-1230 h. After taking light lunch, she moves again well in the second half of the afternoon, leading to blood glucose decrease in the evening. At night, she always relaxes at home, and does not move much after dinner.



**Figure 1** Average blood glucose for 14 days by continuous glucose monitoring (CGM).

The glucose profiles in three different characteristic situations were shown in **Figure 2**. The lifestyle on January 28th was usual and she was working from morning until evening (**Figure 2a**). After taking breakfast, blood glucose increases, decreases before lunch and keeps low during 1200-1230 h. Glucose level was stable in the afternoon, and became low during 1700-1800 h because of continuation of walking. At night, glucose value was stable due to relaxed time at home.



**Figure 2** Blood glucose profile in 3 days by continuous glucose monitoring (CGM). Subject worked 0900h-1800h with regular insulin treatment (2a). Subject did not work all day with regular insulin treatment (2b). Subject worked 1500-2100 h without insulin injection at 1900 h (2c).

She was off on January 30th without work, and did not walk around for the day (**Figure 2b**). Therefore, results with less fluctuation in blood glucose were obtained. The increase in blood glucose after 1530 h was due to intake of sugar-rich cake.

She worked during 1500-2100 h on Feb.1st (**Figure 2c**). Glucose fluctuation during 0900-1230h are compared with **Figures 2a and 2c**. When moving frequently in the morning, blood sugar falls well (**Figure 2a**), but when keeping still, it does not go down (**Figure 2c**). As she started working from 1500 h, blood sugar gradually declined. She took snacks in 1830 h, but she could not inject the insulin on the evening. After that, hyperglycemia persisted for long, although Glargin was given on 2300 h. The hyperglycemia lasted until the next morning, in which blood glucose was 220 mg/dL at 0700 h.

## Discussion

Treatment using real-time CGM (rtCGM) associated with multiple daily insulin (MDI) injection confers similar or greater benefits for glycemic profile [16]. Moreover, there have been lots of studies that use of rtCGM could improve glycemic control in children and adults with T1DM [17-20]. The beneficial points of rtCGM are found in cases who wear CGM devices more frequently and respond to regulate appropriately according to the glucose data provided [17,21].

Especially, CGM is clinically important for cases with T1DM on MDI injection [22]. CGM has the potential benefits of effective use of glycemic rate of change (ROC) arrows for dose adjustments of insulin [23].

As to the insulin treatment, pre-meal glycemic slope predicts post-meal glycemic excursions and may help inform insulin dosing decisions. Rate-of-change arrows on existing devices obscure clinically actionable glycemic trend information from CGM users [24].

CGM devices have developed over the past years for the standard care for patients with T1DM [25]. Compared with the traditional blood glucose monitoring (BGM), recent CGM data represent 24-hour glycemic variability and prediction of glucose changes simultaneously. Recently, there has been broader application for patients with various states [26]. Furthermore, Food and Drug Administration (FDA) in United States approved the management decisions in 2016 that include insulin dosing from CGM values [27].

CGM devices record interstitial glucose level and have the advantage of providing detail and precise glucose readings, with recently a new generation of implantable variability [28,29]. Furthermore, CGM has shown improvement in glucose variability, measured as HbA1c, reduction of hypoglycemia and cost-effectiveness [30].

Recently, clinical practice guidelines have been generally simplified the criteria for CGM use by the endocrine society [31]. According to the data from 11 RCTs using CGM for T1DM, CGM would alter HbA1c (95% CI) by -0.28% (-0.47, -0.09), and reduces the risk of hypoglycemia, particularly with lower HbA1c levels [31].

As for T1DM case studied in this study, there seemed to be three characteristic findings. Firstly, blood glucose increased during 0800-1000 h, which is probably due to rather excess intake of carbohydrate or shortage of rapid effective insulin. Secondly, blood glucose was decreasing due to the effect of continuous physical movement. It is from her lifestyle and habit that she always moves and walks around without sitting during working.

Thirdly, when insulin injection was not done at 1900h, hyperglycemia has lasted overnight. In this point, blood glucose increased from 76 to 396 mg/dL, ie., rise of 320 mg/dL. In T1DM, there is averagely an increase of 5 mg/dL of blood glucose per 1g of carbohydrate intake. Then the ingested sugar amount was calculated to be about 64 g. Ingested carbohydrate was actually 72 g, which seemed to be roughly consistent.

## Conclusion

As to this investigation, blood glucose profile can be clarified in detail by application of CGM, indicating clinical usefulness. Furthermore, it is possible to recommend the timing and dose of insulin injection according to the lifestyle of the patient, suggesting a great clinical merit. These results would be useful as basic data for better treatment and clinical research in T1DM.

## Supplement

This study was conducted in compliance with the ethical principles of the Declaration of Helsinki. In addition, it was with Japan's Act on the Protection of Personal Information along with the Ministerial Ordinance on Good Clinical Practice (GCP) for Drug (Ordinance of Ministry of Health and Welfare No. 28 of March 27, 1997). We held ethical committee meeting including physicians, nurse, pharmacist, clinical engineer and academic experts. Informed consent was obtained from the subject.

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