Bando et al., Clin Med Case Rep 2018, 2:1

Clinical and Medical Case Reports

Case Report Open Access

Glucose Profile and HbA1c using Continuous Glucose Monitoring (CGM): Case Report

Hiroshi Bando[1,2*], Koji Ebe[2,3], Yoshikane Kato[4], Setsuko Kanazawa[4], Mayumi Tanaka[4], Etsuko Sueki[4], Hiroe Kanagawa[4], Takafumi Kawata[4], Atsuko Kawahito[4], Masahiro Bando [5] and Yoshikazu Yonei[6]

[1]Medical Research, Tokushima University, Tokushima, Japan

[2]Low Carbohydrate Diet Promotion Association, Kyoto, Japan

[3]Takao Hospital, Kyoto, Japan

[4]Kanaiso Hospital, Tokushima, Japan

[5]Department of Nutrition and Metabolism, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan

[6]Anti-Aging Medical Research Center, Graduate School of Life and Medical Sciences, Doshisha University, Kyoto, Japan

[*]**Corresponding author:** Hiroshi Bando, Medical Research, Tokushima University, Nakashowa, Tokushima, Japan, Tel: +81-90-3187-2485; E-mail: pianomed@bronze.ocn.ne.jp

Received Date: 18 December 2017; **Accepted Date:** 09 January 2018; **Published Date:** 18 January 2018.

Abstract

Background: Continuous Glucose Monitoring (CGM) has been in focus for treatment of diabetes. Recently, a sensor-based flash glucose monitoring system, FreeStyle Libre (Abbott), has been introduced to clinical practice.

Case and results: The patient was 53 year-old female with type 1 diabetes mellitus (T1DM), who showed BMI 25.1 kg/m^2, HbA1c 9.5% in January, 6.0% in June and 7.7% in November, 2017 as data on outclinic. CGM measured glucose every 15 minutes in 24 hours for 14 days on June and November, and estimated HbA1c was 5.4% and 6.1%, respectively with discrepancy.

Discussion and conclusion: The beneficial points of FreeStyle Libre have been accurate, convenient and small size for clinical use for lessen hypoglycemia episodes. Key benefits of CGM monitoring are frequency of testing, trends, alarms, therapy optimization. Former studies for FreeStyle Libre tended to show lower values and larger mean absolute relative difference (MARD) in lower range of glucose levels, suggesting possible cause of the discrepancy for HbA1c levels. FreeStyle Libre for CGM would lead to better balance optimization of glucose control and current results would become basal data for future investigation of CGM.

Keywords: Continuous glucose monitoring; FreeStyle libre; Type 1 diabetes mellitus; Mean absolute relative difference; Low carbohydrate diet

Abbreviations

CGM: Continuous Glucose Monitoring; T1DM: Type 1 Diabetes Mellitus; MARD: Mean Absolute Relative Difference; DCCT: Diabetes Control and Complications Trial; EDIC: Epidemiology of Diabetes Interventions and Complications; LCD: Low Carbohydrate Diet; M: Morbus value; CLSI: Clinical and Laboratory Standards Institute; MARD: Median Absolute Relative Deviation; PARD: Precision Absolute Relative Difference; SC-CGM: Subcutaneous Continuous Glucose Monitoring System; MD-CGM: Microdialysis Continuous Glucose Monitoring System

Introduction

The importance of controlling diabetic states has been emphasized by several mega study such as Diabetes Control and Complications Trial (DCCT) and Epidemiology of Diabetes Interventions and Complications (EDIC) [1,2]. One of the effective research methods would be the profile of blood glucose. Authors have reported clinical studies concerning low carbohydrate diet (LCD) and investigated glucose profile and related Morbus (M) value, indicating the efficacy of LCD [3,4]. We also investigated the clinical significance of ketone bodies in fetus, placenta, newborn and pregnant mother in the light of LCD and glucose metabolism [5].

Continuous Glucose Monitoring (CGM) has been in focus for better treatment of diabetes. CGM was reported at first by Updike et al. [6]. After that, electrodes for converting blood glucose concentration into electric signals were devised, and several trials for CGM were developed [7].

Consequently, Clinical and Laboratory Standards Institute (CLSI) showed the guideline for CGM [8]. Consequently, reports have been proposed concerning international standardization such as median absolute relative deviation (MARD) and precision absolute relative difference (PARD) [9,10].

Recently, a sensor-based flash glucose monitoring system has been introduced to clinical practice using the flash glucose-sensing technology, which is FreeStyle Libre (Abbott, USA) [11,12]. In this study, blood glucose of patient with type 1 diabetes mellitus (T1DM) was measured by FreeStyle Libre twice and investigated in detail.

Case Presentation

The patient was 53 year-old female with type 1 diabetes mellitus (T1DM) treated with insulin therapy for more than 10 years. She was in rather uncontrolled condition during 2016 with the HbA1c from 9.1% to 11.5%. From January 2017, she was treated with our diabetic program including both insulin therapy and education of carbohydrate influence for blood glucose, which has been our medical and social activity and movement for low carbohydrate diet (LCD) for several years.

On physical examination, she showed 152 cm in height, 58 kg in weight, BMI 25.1 kg/m^2, abdominal circumference 89 cm, thigh circumference 40 cm. Her vitals and consciousness are normal, and lung, heart, abdomen and neurological findings were unremarkable. Laboratory data on January 2017 were as follows: postprandial blood glucose on 120 min. was 242 mg/dL, and HbA1c was 9.5%, AST 19 IU/mL, ALT 23 IU/mL, r-GT 25 IU/mL, Alb 4.6 mg/dL, Cre 0.64 mg/dL, Hb 15.4 g/dL, TSH 0.81 μIU/mL, free T4 1.26 ng/dL, HDL 37 mg/dL, LDL 89 mg/dL, TG 215 mg/dL.

The changes of postprandial blood glucose, HbA1c, insulin treatment and body weight during 11 months are shown in Table 1. HbA1c value decreased to 6.0% in June 2017, and after that increased to 7.7% in November.

Time											
Month in 2017	1	2	3	4	5	6	7	8	9	10	11
Glucose Examination											
Glucose-2 h (mg/dL)	242	140	123	184	123	109	95	108	182	194	165
HbA1c (%)	9.5	8.4	7.9	7.1	6.6	6.2	6	6.7	7.1	7.4	7.7
Insulin Treatment											
Apidora 07 h (unit)	23	23	22	19	16	12	9	10	11	13	16
Apidora 12 h (unit)	25	26	25	23	21	12	9	11	13	15	19
Apidora 18 h (unit)	25	26	24	22	20	14	11	13	14	16	19
Lantas 22 h (unit)	25	26	25	25	24	22	17	19	21	23	26
Body Weight											
Body weight (kg)	58.5	56	55.7	55.5	54.6	55.7	55.2	54.9	55.2	56.3	56.9

Table 1: Changes of glucose, HbA1c and insulin treatment of the case.

CGM was performed twice in June and November in 2017 (Figure 1). We measured blood profile every 15 minutes in 24 hours for 14 days using FreeStyle Libre. It showed the changes of blood glucose precisely. However, HbA1c level estimated from the data of CGM was 5.4% and 6.1%, respectively, which showed discrepancy with the HbA1c level measured on outclinic, which was 6.0% and 7.7%, respectively.

Sensor-based device for CGM

The sensor-based device for blood glucose monitoring was the FreeStyle Libre Flash Glucose Monitoring system, produced by Abbott Diabetes Care Inc, Alameda, CA, USA.

Its system was the first commercially available sensor systems using factory-calibrated sensors which is the beneficial point [13,14]. It can indicate for replacing blood glucose testing and detecting trends and tracking patterns aiding in the detection of episodes of hyperglycemia and hypoglycemia. Its characteristic points are accurate, convenient and small size for clinical use [12,15]. The sensor is worn on the back of the arm for up to 14 days and automatically stores glucose data every 15 min [11,12,16,17].

Discussion

As to the treatment of T1DM, majority (>75%) of pediatric patient do not meet International Society for Pediatric and Adolescent Diabetes / American Diabetes Association guidelines for glycaemic control (glycated Hb, 58 mmol/mol (7.5%) [18]. The problems include HbA1c value and episodes of hypoglycemia which might be in severe risk for life. Using FreeStyle Libre for 139 participants 6 months, hypoglycemia was reduced by 50% with efficacy [16].

Schierenbeck compared and investigated two different CGM-systems [19]. One is FreeStyle Libre subcutaneous continuous glucose monitoring system (SC-CGM) and another is the Eirus intravascular microdialysis continuous glucose monitoring system (MD-CGM). In fact, both were reliable and used without complications [19].

Key benefits of CGM monitoring are frequency of testing, trends, alarms, therapy optimization and diagnosis [14]. Similarly, guideline of CLSI showed 7 important points, which are point accuracy, trend accuracy, alarms, the stability of the sensor, calibration, time lag and traceability [8].

In this study, there were discrepancy of HbA1c values twice. The former was 6.0% vs 5.4%, and the latter was 7.7% vs. 6.1%, respectively. The reason for discrepancy would include the possibilities as follows: 1) less carbohydrate intake due to nutritional education for LCD for months, 2) psychologically less intake of carbohydrate during 14 days

for CGM, 3) difficulty of capture for rapid and short time postprandial hyperglycemia due to every 15 minute interval for CGM, 4) lower glucose values in lower range of blood glucose <100 mg/dL on Libre system (Figure 1).

Accuracy, safety and user acceptability of the FreeStyle libre System were demonstrated for the 89 pediatric patients with T1DM [12]. On contrast, Mean difference (SD) was reported to be -43.4 (20) mg/dL, using FreeStyle Libre SC-CGM [19]. Furthermore, it tended to show lower values in the lower ranges, and the underestimation of the effect of meal on glucose response [20]. The mean absolute relative difference (MARD) of glucose levels in range of <72, 72-180, <181 was 20.3%, 14.7%, 9.6%, respectively [21].

Linear regression analysis between the A1C and average glucose values provided the tightest correlations, indicating the formula that Average glucose (mg/dL) = 28.7 × A1c – 46.7, R2=0.84 [22].

Taking these data into consideration, -43.4 / 28.7 equals to -1.5, in which the estimated A1c calculated from CGM might be 1.5% lower in lower range. From this standpoint, the discrepancy of HbA1c values, at least in part, might be explained.

Conclusion

Diabetic management has been changing worldwide due to clinical application of CGM, leading to better balance optimization of glucose control with less risks of hypoglycemia [23]. The results in this study would become basal data for future investigation of CGM in diabetic patients.

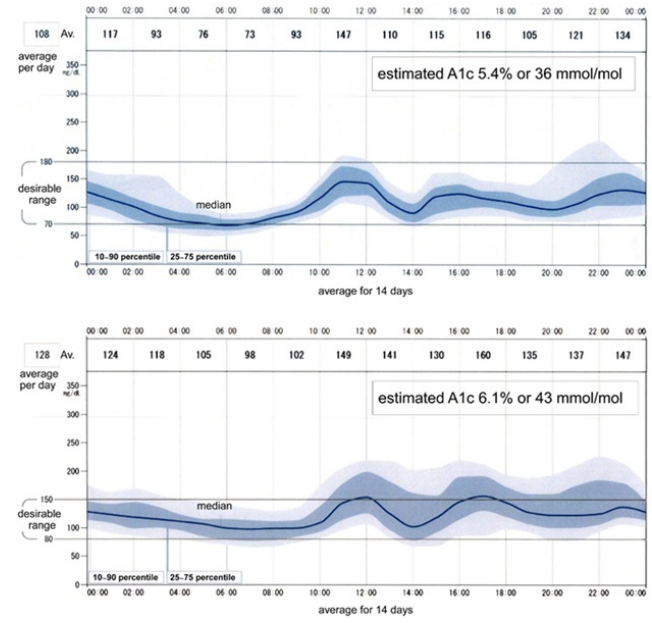

Figure 1: Results of continuous glucose monitoring (CGM). a) CGM data for 14 days in June, 2017. Estimated 5.4% in HbA1c showed discrepancy with 6.0% in ordinary measurement in outlinic. b) CGM data for 14 days in November, 2017. Estimated 6.1% in HbA1c showed discrepancy with 7.7% in ordinary measurement in outlinic.

Acknowledgement

Current study was conducted in compliance with the ethical principles of the Declaration of Helsinki and 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). Ethical committee meeting was held including physicians, nurse, pharmacist, clinical engineer and academic experts. Informed consent was obtained from the subject.

Conflicts of Interest

The authors would like to thank the patients and staffs for their cooperation and support. The authors declare that they have no conflicts of interest.

References

1. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, Lachin J, Cleary P, et al. (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 329: 977-986.
2. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, et al. (2005) Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med 353: 2643-2653.
3. Bando H, Ebe K, Muneta T, Bando M, Yonei Y (2017) Effect of low carbohydrate diet on type 2 diabetic patients and usefulness of M-value. Diabetes Res Open J 3: 9-16.
4. Ebe K, Bando H, Muneta T, Bando M, Yonei Y (2017) Effect of low carbohydrate diet (LCD) for diabetic patients with hypertriglycemia. Endocrinol Metab 1: 104.
5. Muneta T, Kawaguchi E, Nagai Y, Matsumoto M, Ebe K, et al. (2016) Ketone body elevation in placenta, umbilical cord, newborn and mother in normal delivery. Glycative Stress Research 3: 133-140.
6. Updike SJ, Hicks GP (1967) The enzyme electrode. Nature 214: 986-988.
7. Skyler JS (2009) Continuous glucose monitoring: an overview of its development. Diabetes Technol Ther 11: S5-10.
8. https://clsi.org/media/1502/poct05a_sample.pdf
9. Obermaier K, Schmelzeien-Redeker G, Schoemaker M, Klötzer HM, Kirchsteiger H, et al. (2013) Performance evaluations of continuous glucose monitoring systems: precision absolute relative deviation is part of the assessment. J Diabetes Sci Technol 7: 824-832.
10. Liebl A, Henrichs HR, Heinemann L, Freckmann G, Biermann E, et al. (2013) Continuous glucose monitoring working group of the working group diabetes technology of the German diabetes association: Continuous glucose monitoring : evidence and consensus statement for clinical use. J Diabetes Sci Technol 7: 500-519.
11. https://www.freestylelibre.us/
12. Edge J, Acerini C, Campbell F, Hamilton-Shield J, Moudiotis C, et al. (2017) An alternative sensor-based method for glucose monitoring in children and young people with diabetes. Arch Dis Child 102: 543-549.
13. Hoss U, Budiman ES (2017) Factory-calibrated continuous glucose sensors: The science behind the technology. Diabetes Technol Ther 19: S44-S50.
14. Slattery D, Choudhary P (2017) Clinical use of continuous glucose monitoring in adults with type 1 diabetes. Diabetes Technol Ther 19: S55-S61.
15. Sekido K, Sekido T, Kaneko A, Hosokawa M, Sato A, et al. (2017) Careful readings for a flash glucose monitoring system in nondiabetic Japanese subjects: individual differences and discrepancy in glucose concentrarion after glucose loading. Endocr J 64: 827-832.

16. Haak T, Hanaire H, Ajjan R, Hermanns N, Riveline JP, et al. (2017) Use of flash glucose-sensing technology for 12 months as a replacement for blood glucose monitoring in insulin-treated type 2 diabetes. Diabetes Ther 8: 573-586.
17. Bailey T, Bode BW, Christiansen MP, Klaff LJ, Alva S (2015) The performance and usability of a factory-calibrated flash glucose monitoring system. Diabetes Technol Ther 17: 787-94.
18. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, et al. (2015) Current state of type 1 diabetes treatment in the US: Updated data from the T1D exchange clinic registry. Diabetes Care 38: 971-978.
19. Schierenbeck F, Franco-Cereceda A, Liska J (2017) Accuracy of 2 different continuous glucose monitoring systems in patients undergoing cardiac surgery. J Diabetes Sci Technol 11: 108-116.
20. Fokkert MJ, Van Dijk PR, Edens MA, Abbes S, de Jong D, et al. (2017) Performance of the FreeStyle Libre Flash glucose monitoring system in patients with type 1 and 2 diabetes mellitus. BMJ Open Diabetes Res Care 5: e000320.
21. Ólafsdóttir AF, Attvall S, Sandgren U, Dahlqvist S, Pivodic A, et al. (2017) A clinical trial of the accuracy and treatment experience of the flash glucose monitor freestyle libre in adults with type 1 diabetes. Diabetes Technol Ther 19: 164-172.
22. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, et al. (2008) Translating the A1c assay into estimated average glucose values. Diabetes Care 31: 1473-1478.
23. American Diabetes Association (2017) Standards of medical care in diabetes 2017. Diabetes Care 40: S52.