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Case Report

Glucose-lowering efficacy of Xultophy with low doses by FreeStyle Libre as continuous glucose monitoring (CGM)

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Abstract

The daily profile of blood glucose can be detected by continuous glucose monitoring (CGM) using FreeStyle Libre. The case was a 51-year-old female with type 2 diabetes mellitus (T2DM) for uncontrolled glucose variability as HbA1c 10.3%. During CGM measurement, diabetic treatment was changed from multiple daily insulin injections (MDI) to Xultophy (insulin degludec and liraglutide). Xultophy starting from 10 to 18 doses has brought the improvement of glucose variability, such as decreased pre-prandial glucose from 268 mg/dL to 101 mg/dL. Consequently, detailed data of glucose variability on Xultophy using CGM would be beneficial and become some reference for further clinical diabetic research.

Keywords: continuous glucose monitoring; FreeStyle Libre; Xultophy

1. Introduction

Type 2 diabetes mellitus (T2DM) and/or metabolic syndrome have been crucial medical and economic problems [1]. The prevalence of diabetes worldwide is increased and some adequate strategies would be required [2]. Adequate therapy has been necessary and standards of diabetic medical care and cure have been proposed by American Diabetes Association (ADA) [3].

As to diabetic practice, there have been recent topics concerning nutritional therapy and technical examination. For diet treatment, meaningful changes have been found. The standard therapy was formerly calorie restriction (CR), which was calculated by the total calorie of food intake [4]. However, a low carbohydrate diet (LCD) has been introduced to health care and medical practice by Bernstein and others [5]. The clinical efficacy of LCD has been reported by several investigators in European and North American countries [6,7]. On the other hand, the authors have started the movement for LCD in Japan in 2000 [8]. After that, we have established the Japan LCD promotion association (JLCDPA) and proposed three types of LCD, which are super-LCD, standard-LCD, and petite-LCD for practical use [9]. We developed medical and social influences for informing the significance of LCD [10]. Furthermore, we have continued clinical

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research of LCD concerning the daily profile of blood glucose, elevated Beta-Hydroxybutyrate (BHB), Morbus value, meal tolerance test (MTT), and continuous glucose monitoring (CGM) [11].

Regarding technological medical development, CGM has played an important role in controlling glucose variability [12,13]. CGM was originally introduced to clinical practice as a sensor-based measurement for blood glucose in a diabetic patient [14]. Its brand name is FreeStyle Libre, and it has been estimated to be reliable to measure the daily profile of blood glucose [15]. The reason includes the simplicity and usefulness for monitoring the detail changes of blood fluctuation with convenient manual and small size [16].

Our medical group has continued diabetic practice and research for a long. We have treated diabetic patients with various complications and situations. Among them, we experienced a diabetic case showing a significant effect of Xultophy, which is the combination of two agents of insulin degludec and liraglutide. The detailed changes in blood glucose could be monitored by CGM. In this article, the case will be presented with some discussion.

2. Case Report

The case was a 51-year-old female with T2DM. She has a diabetic history of about eight years, and continued insulin therapy for five years. The method was multiple daily injections (MDI), and she was provided long-acting and rapid-acting insulin. The agents included insulin Glargine once at night and NovoRapid three times a day before meals. Recently, she had used Glargine 14 units and NovoRapid 18,15,18 units per day.

Her physical examination showed as follows: height 153 cm, weight 60 kg, BMI 25.6 kg/m², abdominal circumference 90 cm. Vitals are unremarkable, consciousness and speech are normal. Lung, heart, abdomen, and neurological conditions were unremarkable.

Laboratory examination revealed that Hb 14.1 g/dL, GOT 19 IU/mL, GPT 18 IU/mL, r-GT 22 IU/mL, Alb 4.8 g/dL, Cre 0.7 mg/dL, HDL 39 mg/dL, LDL 103 mg/dL, TG 198 mg/dL, post-prandial blood glucose 293 mg/dL, and HbA1c was 10.3 %.

As to her clinical course, HbA1c values were higher by more than 10% from November to December 2020. Then, we have tried to evaluate the detailed glucose variability using FreeStyle Libre and to start the administration of Xultophy instead of the MDI method.

2.1. FreeStyle Libre

The examination of glucose variability was conducted by FreeStyle Libre, which was produced by Abbott Diabetes Care Inc, Alameda, CA, USA [14]. It was first introduced to medical practice for CGM with factory-calibrated sensors [16]. Its characteristic merits have been convenient, accurate, and simple [15]. The sensor can be set on the back of the upper arm, automatically measuring glucose values every 15 min for 24 hours during 14 days [17].

2.2. Results

The obtained data of CGM in the case were shown in Figure 1. The blood glucose was studied for 14 days. For the first three days, she was given the previous treatment of MDI. During that time, the daily profile of glucose showed higher especially in post-prandial glucose with more than 350 mg/dL. From 4 to 14 days, she was provided Xultophy starting 10 doses increasing up to 18 doses. During the period, the daily profile of glucose was gradually decreased, which was indicated by the red arrows in Figure 1. In the evening, pre-prandial blood glucose decreased from 268 mg/dL to 101 mg/dL.

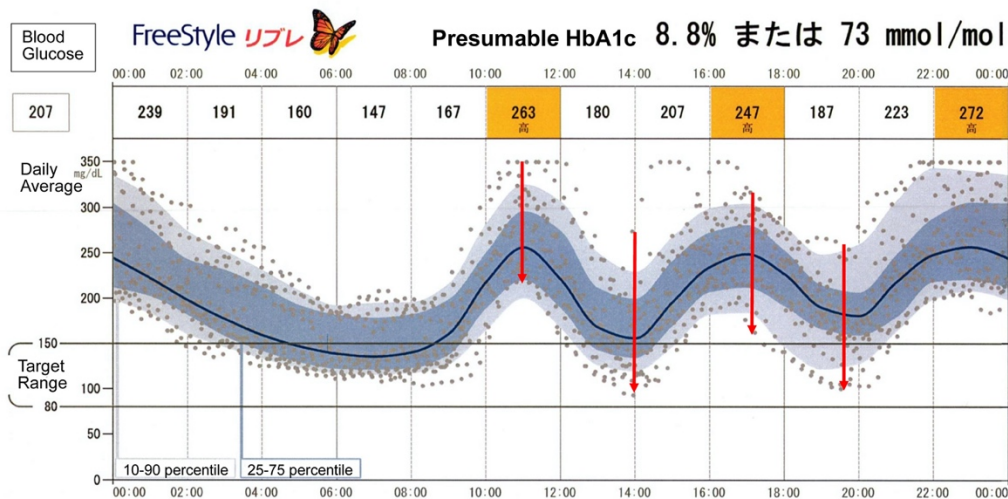


Figure 1. The changes in the daily profile of blood glucose using FreeStyle Libre as CGM. Preprandial and postprandial glucose values have decreased as shown in red arrows.

3. Discussion

In the current study, the performance of CGM was successful. Improvement of the daily profile of blood glucose was found in two weeks. It is beneficial to obtain actual glucose fluctuation in both pre-prandial and post-prandial periods. Thus, the study of glucose variability using FreeStyle Libre seems to be beneficial and satisfactory.

However, it is unlikely that the HbA1c value calculated from the computer software of FreeStyle Libre equals that of HbA1c in the out clinic. The values from FreeStyle Libre seem to be usually lower than those in the out clinic. In this case, HbA1c in the out clinic was 10.3%, while datum from Libre was 8.8% indicating a 1.5% difference. Such a phenomenon has been reported before [18]. One of the reasons would be from the measuring mechanism, where CGM cannot catch up with the abrupt elevation of blood glucose. Continuous blood glucose values can be detected every 7.5 to 15 minutes by two devices of FreeStyle Libre and Freestyle Libre Pro [19]. Another possible factor would be the fact that Libre can detect the glucose level, not in the venous vessel but the interstitial fluid. Consequently, the HbA1c value calculated from Libre would be the reference data among fluctuating glucose situations.

In this study, the case with T2DM has changed the treatment from MDI to Xultophy. Xultophy includes the combined function of two agents, which are long-acting insulin and GLP-1RA. Regarding the doses of Xultophy, 1 dose contains 1 unit of insulin degludec and 0.036 mg of liraglutide [20]. The standard usage of Xultophy shows that the patient may be given 10 to 50 doses. An injectable pen is prefilled by 300 doses including 100/3.6, which means insulin degludec 300 units, and liraglutide 10.8 mg. This pen has no push-button extension, and the doses button will not extend when dialing behavior is on the way [15,20]. It can be administered once per day, and it reveals less possibility of increased weight or an episode of hypoglycemia compared with other insulin therapy. Furthermore, it shows less adverse effects of gastrointestinal symptoms in comparison with GLP-1RA injection alone [15,20,21].

As to the starting doses, the insulin-naïve patient begins at 10 doses, while the patient having experience of insulin begins at 16 doses. On the other hand, our medical team has several experiences in providing Xultophy so far. There are T2DM patients with various backgrounds and complications. In such cases, we tried to start Xultophy at the level of 5 doses. Then, some cases could be controlled at the levels of 5-14 doses. It may be from the small physique of the Japanese race, different degrees of response for GLP-1RA, compliance of treatment, adherence of medical agent, regular lifestyle, and so on [21].

The investigation of clinical response of Xultophy was present, which is the European Xultophy Treatment Retrospective Audit (EXTRA) study. From European diabetes centers, a real-world evidence (RWE) study (EXTRA) was reported. The result showed a significant decrease of HbA1c value (-0.7%) and also of weight (-2.4 kg) for six months in the subjects who changed from MDI to Xultophy [22]. Related to the EXTRA study, a large investigation included 611 cases from five countries. As a result, the initiation therapy showed a substantial -0.9% reduction of HbA1c ($p < 0.001$) after six months [23]. Consequently, Xultophy seems to be a beneficial and convenient agent for T2DM associated with the adequate continuation of a regular lifestyle. In the current case, she has occasionally rather irregular diet behavior and the medical staff will give some advice for maintaining stable daily life.

In summary, a female patient with T2DM showed uncontrolled diabetic states. Then, she has checked the daily profile of blood glucose using FreeStyle Libre as CGM method and has changed to Xultophy from 10 to 18 doses associated with satisfactory control of glucose variability. This report hopefully becomes one of the references for CGM and Xultophy in the future.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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