



Significant Effect of Improved Glucose Variability by Standard Low Carbohydrate Diet (LCD) and EquMet

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Abstract

The case is 69-year-old male with Type 2 diabetes (T2D). He developed the swelling and redness of right thumb in Jan 2024, and visited the hospital. He was diagnosed as T2D for HbA1c 14.7% and blood glucose 559 mg/dL. Treatment started immediately by standard low carbohydrate diet (LCD) and metformin/vildagliptin (EquMet) LD to EquMet HD. Standard LCD means limited carbohydrate for 26% of calorie ratio by Japan LCD promotion Association (JLCDPA). HbA1c decreased linearly to 6.3% for 6 months, and mean amplitude of glycemic excursions (MAGE) was improved. Thus, combination of LCD and EquMet can bring remarkable clinical effect.

Keywords: Metformin/vildagliptin (EquMet); Standard low carbohydrate diet (LCD); Japan LCD promotion Association (JLCDPA); Mean amplitude of glycemic excursions (MAGE); Vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY)

Introduction

Across the world, clinical problem of type 2 diabetes (T2D) has become crucial for decades [1]. For management of T2D, standard guideline has been introduced from American Diabetes Association (ADA) [2]. T2D show various complications because of the damage of all blood vessels in the body, then the protection of arteriosclerosis would be required [3]. Then, adequate treatment for stabilizing the daily fluctuation of blood glucose is mostly indispensable.

For achieving better glucose variability, improvement of daily diet pattern will be necessary. For diet therapy, previous standard measure was calorie restriction (CR), but low carbohydrate diet (LCD) was introduced to health and medical region by Atkins and Bernstein [4,5]. LCD has been evaluated to be useful measure for patients of obesity and diabetes [6,7]. Authors and research group have continued diabetic practice and research concerning LCD [8].

As pharmacotherapy, oral hypoglycemic agents (OHAs) have been developed and introduced to diabetic practice. Among them, metformin has been for long the first-line agent and dipeptidyl-peptidase 4 inhibitors (DPP4-i) has been known as effective and safe agent. Among them, useful and effective combination includes metformin and DPP4-i for vildagliptin/metformin (EquMet). For this clinical evaluation, large international studies have been conducted, which was vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY) [9]. The prescription of intensified combination has brought a new paradigm shift for the diabetology. Furthermore, recommended diabetic treatment would be presented by ADA and European Association for the Study of Diabetes (EASD) [10].

Authors have treated various T2D patients for long [11]. Recently, we have come across an impressive case, who showed significant improvement by LCD and OHA. Its general clinical progress and related perspectives will be presented in this article.

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Presentation of Cases

Medical History

The current case has been a 69-year-old male with T2D. He was pointed out to have type 2 diabetes (T2D) about 5 years ago. He received diabetic treatment for 3 years, but he was not treated at all for recent 2 years. He has been working in the cleaning service company. He noticed the redness and swelling of right thumb in late January 2024, and visited our hospital in early February (Figure 1). He was diagnosed as MP arthritis and was treated with antibiotics. By the blood chemistry exam, he was diagnosed as severe situation of T2D with HbA1c 14.7% and blood glucose 559 mg/dL. His body weight was 78kg at the age of 20, and increased to the maximum of 90kg about 5 years ago, followed by current weight of 83.7 kg this time.

Table 1: Changes in biochemistry results.

	2024 Feb	Units
Liver		
AST	14	(U/L)
ALT	21	(U/L)
GGT	26	(U/L)
Renal		
UA	4.7	(mg/dL)
BUN	14	(mg/dL)
Cre	0.71	(mg/dL)
Lipids		
HDL	50	(mg/dL)
LDL	114	(mg/dL)
TG	144	(mg/dL)
CBC		
WBC	74	($\times 10^3/\mu\text{L}$)
RBC	500	($\times 10^4/\mu\text{L}$)
Hb	15.9	(g/dL)
PLT	17.6	($\times 10^4/\mu\text{L}$)
Inflam.		
CRP	1.0	(mg/dL)

Physicals and exams

The physical examination showed in the followings: consciousness, speech, facial expression and vital signs were negative, where pulse 82/min, BP 131/93, SpO₂ 98%. His head, lung, heart, abdomen and neurological findings were unremarkable. His right thumb showed swelling. His physique revealed height 174.2 cm, weight 83.7 kg and BMI 27.6 kg/m². His chest X-ray and electrocardiogram (ECG) was within normal limits.

The results of biochemical blood test were summarized in Table 1. They were unremarkable findings in the liver, lipids, renal and complete blood count (CBC), whereas CRP value was elevated.

He received the arteriosclerotic test of pulse wave velocity (PWV) (Figure 2). The level of cardio-ankle vascular index (CAVI) was 9.1/9.6 which was slightly elevated, indicating the presence of arteriosclerosis, and ankle brachial index (ABI) was 1.12/1.10.

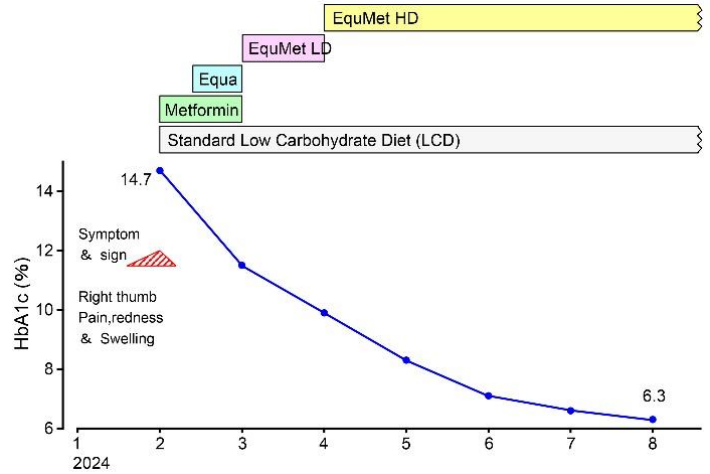


Figure 1: Clinical progress of current case.

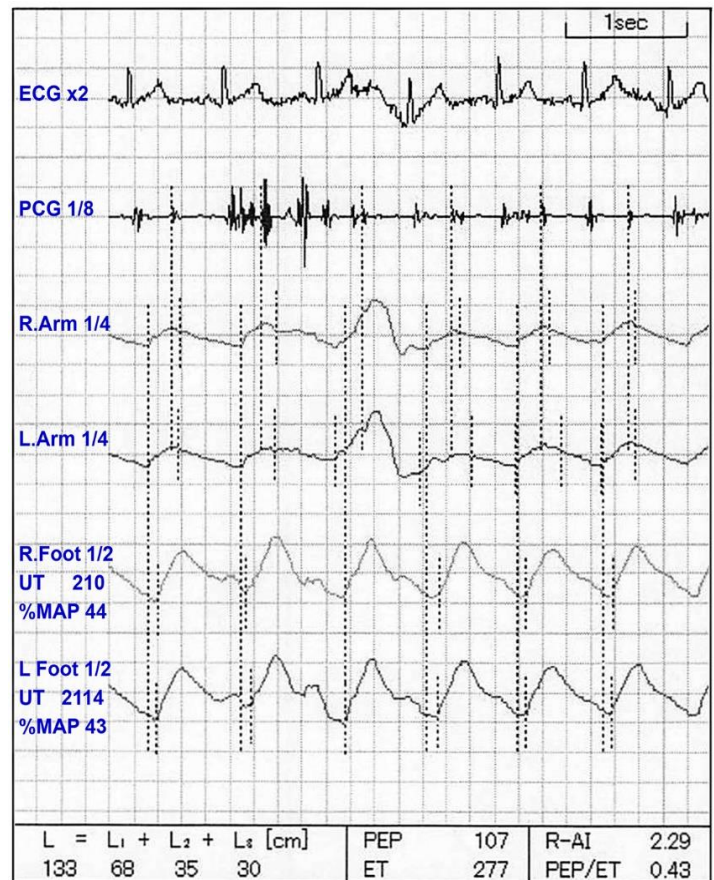


Figure 2: Pulse wave velocity (PWV) test.



Brain MRI

Brain MRI showed mild cerebral atrophy and ventricular enlargement, but the changes are within age-related ranges. No major vascular disorders, lesions or other abnormal changes are found in the brain parenchyma. MRA shows some noticeable vascular tortuosity, and the signals at the branching points seem to be slightly uneven. However, no significant stenosis or aneurysms are found in the main trunk. In the neck, the signals at the origin of the internal carotid artery are observed to be slightly uneven. Generally, these findings seemed to be negative for the age.

Clinical progress

After he was evaluated current situation, he was advised to start low carbohydrate diet (LCD). Discussing fully with him concerning the actual lifestyle, the standard LCD was applied and started. Successively, some kinds of oral hypoglycemic agents (OHAs) were gradually added aiming for satisfactory clinical effect. For OHAs, metformin was given at first, followed by Equa, EquMet LD, and EquMet HD (Figure 1). His HbA1c showed acute reduction with remarkable clinical efficacy. Six months later, HbA1c was 6.3% and his diet style of standard LCD has been satisfactory continued.

Ethical standards

This case report complied with the ethic guideline for previous Declaration of Helsinki [12]. In addition, some comments were observed with the protection regulation. This principle was along with the ethical regulation for clinical practice for human. Some guidelines are from Japanese Ministry, where they are Ministry of Health, Labor and Welfare and Ministry of Education, Culture, Sports, Science Technology. The authors and co-researchers have established ethical committee which is in Sakamoto Hospital, Japan. It has several medical and legal persons, including hospital director, doctors in charge, nurse, pharmacist, registered dietician and legal professional. These members have fully discussed for this case, and agreed the protocol of the research. The informed consent was taken from the patient by the document.

Discussion

This case is 69-year-old patient with T2D, who skipped diabetic therapy for 2 years. He started the nutritional treatment applying the standard LCD, which seemed to be clinically effective. Furthermore, gradually strengthening OHA was likely to be successful, because his HbA1c showed linear reduction for 6 months. Some perspectives are described concerning LCD treatment and combined treatment of Metformin and Vildagliptin (EquMet).

From historical point of view, LCD was initiated by Atkins and Bernstein. After that, Shai reported the comparison of LCD, calorie restriction (CR) and Mediterranean Diet (MD) in 2008, which was the research of Dietary Intervention Randomized Controlled Trial (DIRECT) Group [13]. By this evidence, ADA has changed the official comments for nutritional therapy [2]. Nowadays, LCD has been evaluated for effective method for short period, but it is rather difficult for continuing it for years [14]. Then, some recommendation are found, in which starting of LCD and changing to MD afterwards seems to be useful [15]. In addition, other topics include the Paleolithic diet is likely to be considered as one of the combined choice of suitable diet therapy [16].

The current case has applied the standard level of LCD for months. It was successfully situation for this case. LCD has 3 representative levels for actual continuation, which are super LCD, standard and petite method. For their carbohydrate ratio for calorie base, super, standard and petite shows 12%, 26% and 40%, respectively [17]. We have continued social development of LCD in Japan for years, through various activity of Japan LCD promotion Association (JLCDPA) [18]. The methods include books, seminars, medical journals, internet sites and so on [19]. Furthermore, our JLCDPA members have opportunities for developing LCD for various situations [20,21].

For clinical effect of OHA, this case showed remarkable and stable HbA1c reduction for 6 months. For this reason, it may be due to twice administration (bid) of metformin (Metgluco) and vildagliptin (Equa). Several types of DPP4-i agents have been introduced. Among them, bid agents would be beneficial for suppressing the elevation of blood glucose better. From previous report, vildagliptin has showed clinical efficacy of decreasing mean amplitude of glycemic excursions (MAGE) and suppressing nocturnal elevation of glucose fluctuation [22]. This case applied standard LCD, where he always takes certain amount of carbohydrate in the supper at night. From mentioned above, this case may achieve remarkable improvement of HbA1c for half year. Authors et al. have presented several reports for applying LCD [23]. Furthermore, bid type of OHA may be beneficial in the light of the lifestyle of T2D patients from now on [24].

Some limitation may be present for this article. The case is male T2D case treated by standard LCD and EquMet. It is only one case, and clinical effect is not necessarily found in every case. This case has some arteriosclerosis at present, and we will check and follow the diabetic macroangiopathy and microangiopathy for long term period.

In summary, 69-year-old T2D male was described in this article. He showed remarkable diabetic improvement by standard and EquMet administration. Current case will be carefully followed up in the future. This article is expected to become the beneficial reference data for diabetic research and practice.

Conflict of Interest

The authors declare no conflict of interest.

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