

Treatment of Oral Semaglutide (Rybelsus) for Diabetic Patient with Past History of Crohn's Disease

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Abstract

The case is a 49-year-old male with type 2 diabetes (T2D). In his past history, he suffered from Crohn's disease (CD) in his early 20s and underwent surgery for CD, achieving complete remission after that. He was diagnosed with T2D for 7.4% of HbA1c at the health check-up in April 2022. Oral semaglutide (Rybelsus) 3 mg/day was started as glucagon-like peptide-1 receptor agonists (GLP-1 RAs). For only 4 months, HbA1c decreased to 6.2% with 4kg of weight reduction, indicating a satisfactory effect. No gastro-intestinal adverse effects (GI-AEs) were found. Previous reports showed the beneficial effects of GLP-1RAs for patients with T2D and inflammatory bowel syndrome (IBS).

Keywords: Oral Semaglutide (Rybelsus); Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs); Inflammatory Bowel Syndrome (IBS); Gastro-Intestinal Adverse Events (GI-AEs); Crohn's Disease (CD)

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Introduction

As a medical and social problem for decades, type 2 diabetes (T2D) has been a crucial disease worldwide [1]. Recent pharmacological development has brought several types of anti-diabetes agents. They include glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which have been broadly applied to adequate T2D management. GLP-1 RAs can provide T2D patients with improved glucose variability, decreased weight, and decreased risk of cardiovascular and renal function [2]. Among them, semaglutide has been one of the therapeutic measures with remarkable efficacy for improving glucose variability. Oral semaglutide (Rybelsus®) has been a combination of semaglutide and also sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC), which is an absorption enhancer helping the absorption of semaglutide in the stomach. In particular, Rybelsus® has been evaluated to provide remarkable weight reduction. This effect has been known widely by lots of people, and then it gained popularity as an easy shortcut to fitness. Consequently, it may become one of the most important problems in the social, medical, and healthcare fields [3].

GLP-1RA is known to elicit substantial reductions in weight and glycemia for T2D and obesity. However, previous reports suggest that the treatment should be continued to maintain its efficacy. The study was conducted for people with deprescribed GLP-1RA (DeRx) and those with continued GLP-1RA (Rx), and they were compared [4]. As a result, alternate treatments would be potential, such as LCD education supported by telemedicine. Recently, several reports have been observed regarding the relationship between GLP-1RA and various

medical problems of the gastrointestinal (GI) tract. Beneficial clinical influences of GLP-1RA for GI diseases may be present, such as inflammatory bowel syndrome (IBS), short-bowel syndrome, coeliac disease, and intestinal toxicities [5].

The authors' et al. continued diabetic research for years, including T2D, T1D, and other types [6]. For nutritional therapy, we continue to develop low-carbohydrate diets (LCD) medically and socially through our Japan LCD Promotion Association (JLCDPA) [7]. We have recommended LCD methods for three practical patterns: super LCD, standard LCD, and petite LCD [8]. Such lifestyles can contribute to the maintenance and progress of health in medical and health care areas. Thus, we have provided balanced LCD, exercise, and pharmacological treatments [9].

During our diabetic practice and research, we have happened to treat a T2D male patient with a past history of Crohn's disease. We provided him oral semaglutide (Rybelsus), and clinical progress showed satisfactory results with no gastro-intestinal adverse effects (GI-AEs). In this report, his general course and related perspectives will be introduced.

Case Presentation

History & Physical

This is a 49-year-old male patient with T2D. In his past history, he has suffered from Crohn's disease (CD) since he was in his early 20s and had an operation for CD. After that, his gastrointestinal (GI) symptoms were relieved, and no remarkable health problems were observed during his 30s and early 40s. He has been working as an electrician for years, and his daily life has been stable without any problems. Annual

check-ups in his company have been regularly conducted, and no health problems were found until April 2021 (Table 1). During 2019–2021, some biomarkers showed high values, and the HbA1c test was not included in the basic items in the exams.

When he received a health check-up in 2022 with HbA1c included, he happened to be diagnosed with T2D for 7.4% of HbA1c.

Table 1: Changes in Laboratory Data for Years.

Year	2019	2020	2021	2022			2023	
Month	4	4	4	10	4	10	4	10
AST (U/L)	23	26	25	22	18	20	18	19
ALT (U/L)	34	49	42	50	19	26	19	19
GGT (U/L)	54	78	65	70	24	36	24	27
HbA1c (%)	nd	nd	nd	nd	7.4	6.4	6.3	6.1
LDL (mg/dL)	100	111	119	123	119	128	119	119
HDL (mg/dL)	46	50	51	48	64	55	64	58
TG (mg/dL)	476	315	314	398	76	110	76	156
Weight (Kg)	74	73	72	71	70	66	64	63
Rybelsus Tx					—————→			

A physical examination in April 2022 showed as follows: Vitals are stable, and consciousness and speech are normal. The physical status of the head, lung, chest, heart, lung, and abdomen showed negative findings. The neurological exam was intact. His physique showed 168cm in stature, 71kg in weight, and 25.2 kg/m² for BMI.

Some Examinations

The current case showed some positive data in the blood chemistry, which are summarized in Table 1. Otherwise, unremarkable results were noted. The chest X-ray showed negative results for lung and heart, and the ECG showed unremarkable ST-T changes. For the evaluation of arteriosclerosis, he received plethysmography, in which

brachial-ankle pulse wave velocity (baPWV) was 1283/1339 and ankle-brachial index (ABI) was 1.19/1.21 on the right and left sides, respectively. Those data showed a normal range [10].

Clinical Progress

He started oral semaglutide (Rybelsus) at 3 mg/day in April 2022. After that, HbA1c decreased from 7.4% to 6.2% for 4 months (Figure 1). Body weight was decreased from 70kg to 66kg for 4 months. During the winter of 2022, some exacerbations were observed, but glucose variability remained stable from 2023 to 2024. In February 2024, his HbA1c and weight were 6.1% and 63kg, respectively. During his clinical progress for 2 years, he did not feel any gastro-intestinal adverse effects (GI-AEs).

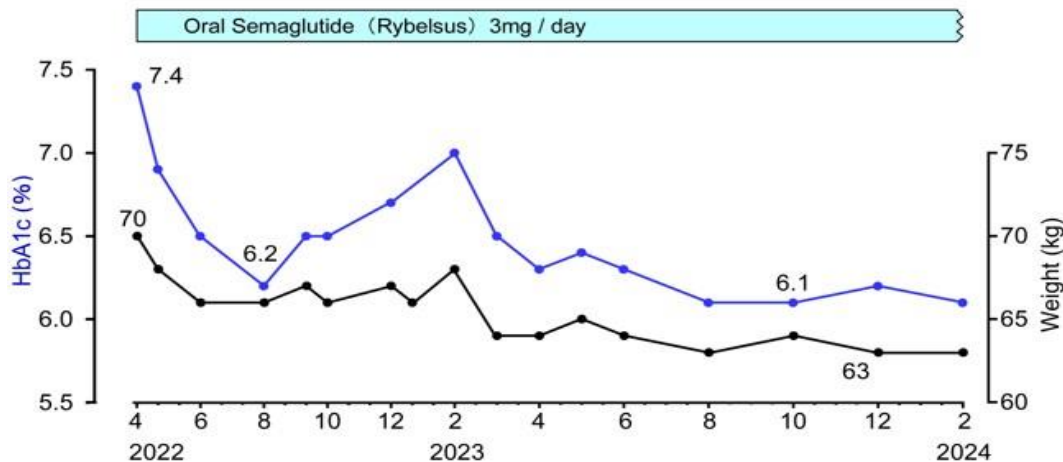


Figure 1: Clinical Progress of the Case for Years.

Discussion

The current case is a T2D male diabetic patient with a past history of Crohn's disease (CD) when he was young. He was treated by Rybelsus at 3 mg/day for a long, and it was not necessary to increase the dose to 7 mg/day or 14 mg/day. Thus, his clinical progress has been satisfactory to obtain good control of glucose variability. Further, he did not have any problems with the GI tract, which is known as the GI-AEs of Rybelsus. Several reports have been found concerning the relationship between Rybelsus and the GI tract.

For patients with T2D and inflammatory bowel disease (IBD), a clinical course followed by GLP-1-based treatment was investigated in 3751 cases [11]. Incidence rate ratios (IRR) were compared for GLP-1RA, DPP-4i, and other antidiabetics. As a result, the adjusted IRR of the outcome showed 0.52 for GLP-1RA/DPP-4i (n = 982) in comparison with those of other therapies (n = 2769). Consequently, these findings suggest that GLP-1RA therapy may improve the clinical progress of those with IBD. According to previous reports, GLP-1 is to regulate some immune responses for the diseased state of immune-mediated diseases, such as CD. Certain research for CD was conducted for the investigation of post-prandial GLP-1 increase and related responses to insulin sensitivity and secretion, chronic inflammation, and physical body composition changes [12]. The protocol included basal GLP-1 level, stimulated GLP-1 secretion level, insulin secretion response, and bio-impedance measurement after the meal tolerance test (MTT). As a result, stimulated GLP-1 secretion was significantly reduced in CD (-31%). The values of hs-CRP and extra-cellular to intra-cellular water ratio (ECW/ICW) showed an inverse correlation with stimulated GLP-1 values.

As part of the current impressive investigation, a SIB trial has been present, which stands for Semaglutide Versus Placebo on Intestinal Barrier Function in Type 2 Diabetes Mellitus [13]. The rationale includes the hypothesis that semaglutide may improve intestinal permeability and also reduce general inflammation in obesity and T2D patients. The participants with T2D showed evidence of systemic inflammation. In several assessments, inflammatory biomarkers include TNF, hs-CRP, IL-1,6,8, HbA1c, fecal calprotectin, lipopolysaccharide-binding protein (LBP), and the lactulose/mannitol ratio test. Thus, SIB is the first investigation examining the efficacy of GLP-1RA on human intestinal permeability and providing meaningful data on systemic inflammatory phenomena for obesity and T2D.

In the latest research, the efficacy of semaglutide on the gut microbiota was investigated [14]. Obese mice were distributed into 4 groups, including those a high-fat diet (HFD) or a normal control diet (NCD), and semaglutide was given or not. As a result, semaglutide influenced the gut microbiota and mitigated microbial dysbiosis by impacting diversity. Consequently, semaglutide may possibly improve the dysbiosis of the gut microbiota, and the gut microbiota may influence the obesity-related clinical efficacy of semaglutide. From a medical

education point of view, an impressive slogan has been known. As to GLP-1RA, the three E's would be essential for the first defense against GI tract problems, such as dyspepsia [15]. They are education, escalation, and effective management. This idea can contribute to the management of patients with GLP-1RA when physicians, nurses, or medical staff can make inquiries about them.

There are limitations to this report. The current case has medical problems with T2D and a past history of CD. He was provided oral semaglutide (Rybelsus), which was effective without any GI-AEs. According to previous reports, GLP-1RA may have a beneficial clinical effect on IBS.

In summary, the current case presents a meaningful suggestion for diabetes and GI function by GLP-1RA. Close attention will be required to follow up on the clinical progress. This article will hopefully become an important reference in future practice and research.

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