

Research Article

The Influence of Blood Glucose Fluctuation Switching from Once-Weekly GLP-1 to Once-Weekly DPP-4 Inhibitors.

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Abstract

Omarigliptin is a new once-weekly DPP-4 inhibitor developed for the treatment of type 2 diabetes. Once-weekly oral administration of omarigliptin reduces dosing frequencies and improves treatment adherence, and potentially contributes to achieving optimal glycemic control compared with once-daily DPP-4 inhibitors. We investigated the effect of omarigliptin on blood glucose fluctuation compared with once-weekly injection dulaglutide in Japanese patients with type 2 diabetes mellitus. Fast blood glucose profiles in Self-Monitoring Blood Glucose (SMBG) were 116.5 ± 10.7 (omarigliptin), and 158.2 ± 43.0 (dulaglutide), respectively. Omarigliptin was initiated with the dose of 25 mg weekly. Blood glucose fluctuation was significantly improved after switching from dulaglutide to omarigliptin.

Keywords: Once-weekly DPP-4 inhibitor; Omarigliptin; Blood glucose fluctuation; anti-diabetic agents; monotherapy

Introduction

Dipeptidyl Peptidase-4 (DPP-4) inhibitors are gaining attention as a novel class of anti-diabetic agents based on the incretin effect. DPP-4 inhibitors achieve glycemic control through inhibition of the DPP-4 enzyme, which contributes to the rapid degradation of incretin hormones, including glucagon-like peptide-1 (GLP-1) and Glucose-Dependent Insulinotropic Polypeptide (GIP). Both of which are released after food intake and then exert glucose-lowering effects through stimulating insulin secretion and by pancreatic β -cell and inhibiting glucagon secretion by pancreatic α -cells in a glucose-dependent manner [1]. Omarigliptin is a new once-weekly Dipeptidyl Peptidase-4 (DPP-4) inhibitor developed for the treatment of type 2 diabetes. It is indicated to have favorable effects on glycosylated hemoglobin A1c (HbA1c), fasting and post meal plasma glucose. In contrast to the once-daily dipeptidyl peptidase-4 inhibitors (e.g., alogliptin, linagliptin, sitagliptin), once-weekly omarigliptin can improve patients' adherence and achieve optimal therapeutic efficacy. In addition, omarigliptin is generally well-tolerated and associated with low risk of hypogly-

cemia. Therefore, omarigliptin provides a useful addition to the therapeutic options for the treatment of patients with type 2 diabetes. To prevent or suppress the progression of diabetic vasculopathies, it is important to minimize glucose fluctuations by lowering postprandial glucose levels and avoiding hypoglycemia, in addition to improvement of HbA1c levels.

Method and Results

We analyzed the data of 3 Japanese patients with type 2 diabetes mellitus who had blood glucose fluctuation under once-weekly DPP-4 inhibitor, omarigliptin. Their average was 73.0 years old, and their baseline HbA1c levels were 6.5%. Blood glucose fluctuation was defined by Self-Monitoring Blood Glucose (SMBG) before meals in all patients. Omarigliptin monotherapy was evaluated with blood glucose profiles obtained from SMBG, as well as HbA1c levels. We used the Standard Deviation (SD) of glucose as the primary outcome measure in the present study. The present study was designed to assess and compare the effects of dulaglutide and omarigliptin on glucose fluctuation. All patients were treated with 0.75 mg weekly dulaglutide and over 20 days later, they were switched to 25 mg weekly omarigliptin. We showed the results of fast blood glucose fluctuation (Figure

1-3). The glucose fluctuation, the SD of glucose levels detected by SMBG, in diabetes patients treated with dulaglutide (158.2 ± 43.0 mg/dl) was markedly and significantly improved by switching to omarigliptin (116.5 ± 10.7 mg/dl).

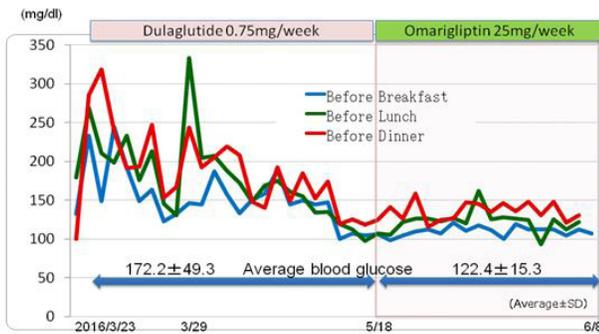


Figure 1: Case 1 - 85 years old, Female - Dementia, under nutrition and edema.

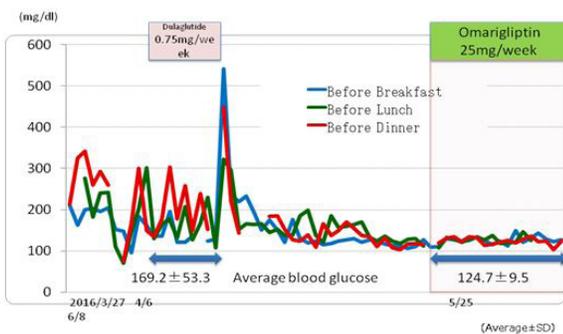


Figure 2: Case 2 - 91 years old, Female - Dementia and loss of appetite.

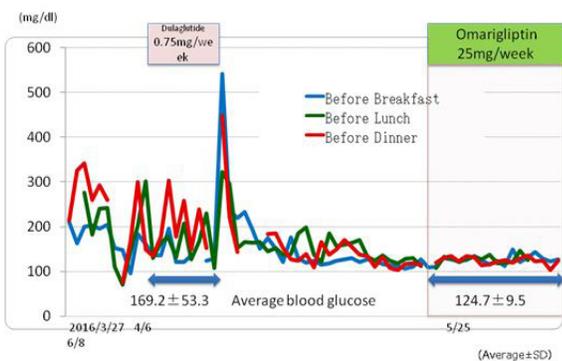


Figure 3: Case 3 - 43 years old. Man - Hemodialysis with type 2 diabetes.

Discussion

DPP-4 inhibitors have been used extensively for the treatment of type 2 diabetes in the last decade, either as monotherapy, or as combination therapy with other anti-diabetic agents. Once-weekly oral medications may simplify the treatment regimen and improve compliance [2]. In September 2015, omarigliptin 12.5

and 25mg once-weekly tablets were approved for the treatment of patients with type 2 diabetes in Japan as monotherapy or combination therapy with other anti-diabetic agents [3]. Oral omarigliptin was generally well-tolerated in patients with type 2 diabetes when administered as monotherapy or in combination with other anti-diabetic agents [4, 5-8]. Omarigliptin is a potent, reversible, competitive DPP-4 inhibitor, and its inhibition constant (K_i) is 0.8 nM [9]. In an oral glucose tolerance test, omarigliptin decreased blood glucose excursion from 0.01 to 0.3 mg/kg (7 % reduction in glucose AUC) to 0.3 mg/kg (51 % reduction) in a dose-dependent manner, the glucose-lowering efficacy of which was similar to that achieved with sitagliptin [9]. In a multicenter, phase 3 study, the mean rate of DPP-4 inhibition was 80.7 % at week 12 following omarigliptin 25 mg q.w. dose compared with the baseline [4]. The increased postprandial 4-h weighed means active GLP-1 level induced by omarigliptin was twice than that by placebo [10]. Population pharmacokinetic data shows that clinical effects are independent to the different sex, age, body weight, or race, which indicates that no dose adjustments are required during omarigliptin therapy on these factors [10]. Omarigliptin is the one of latest DPP-4 inhibitors to reach the market and comparative studies are accordingly necessary to assess its safety in patients with impaired renal function [11]. Glucose fluctuation of omarigliptin was \pm mg/dl, and of dulaglutide was \pm mg/dl. It is important to minimize glucose fluctuations by lowering postprandial glucose levels and avoiding hypoglycemia, in addition to improving HbA1c levels to prevent the progression diabetic macro- and/or microvasculopathy. It is well known that the SD value of glucose reflects glucose fluctuation. We believe that the current report is indicative in clinical practice, because little has been known about the change of blood glucose fluctuation in switching from dulaglutide to omarigliptin. These findings suggested that DPP-4 inhibitors could be expected to lessen glucose fluctuation compared to GLP-1.

Conclusion

Omarigliptin could suppress glucose fluctuation as well as mean glucose levels. Omarigliptin monotherapy was considered to be more effective, and we realize the combination therapy of dulaglutide plus omarigliptin is also potentially useful in clinical medicine.

References

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