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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.

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INTRODUCTION

Dipeptidyl peptidase-4 (DPP-4) inhibitors are gaining attention as a novel class of antidiabetic agents based on the incretin effect. DPP-4 inhibitors achive 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 insulinotrophicpolypeptide (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 (Drucker, 2006). Omarigliptin is a new once-weeklydipeptidyl peptidase-4 (DPP-4) inhibitor developed for the treatment of type 2 diabetes. It is indicated to have favorable effects on glycosylated hemoglobinA1c (HbA1c), fasting and postmeal 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 hypoglycemia. 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.

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METHODS 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 was73.0 years old, and their baseline HbA1clevels 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 weeklyomarigliptin. 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).

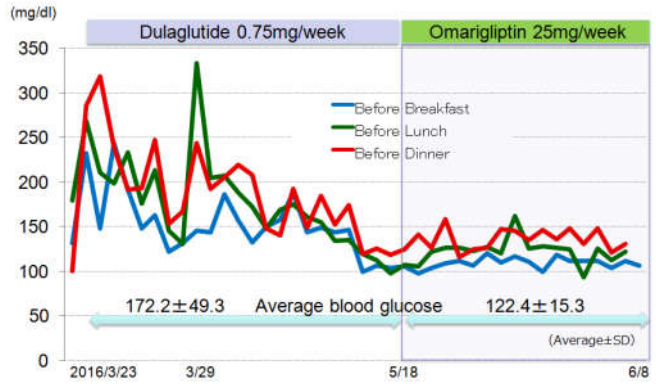

Figure 1.Case 1. 85 years old. Female Dementia, undernutrition and edema

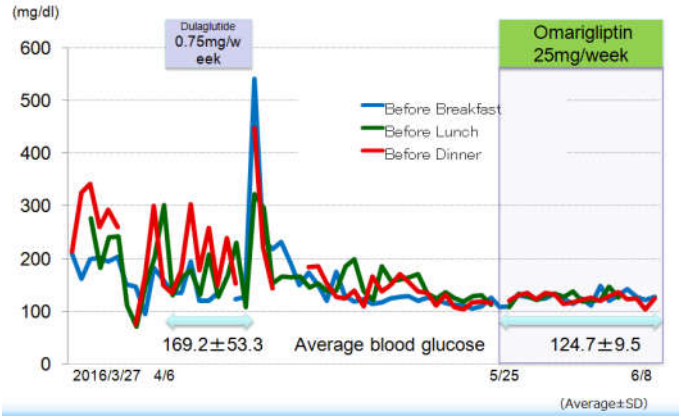

Figure 2. Case 2.91 years old. Female Dementia and loss of appetite

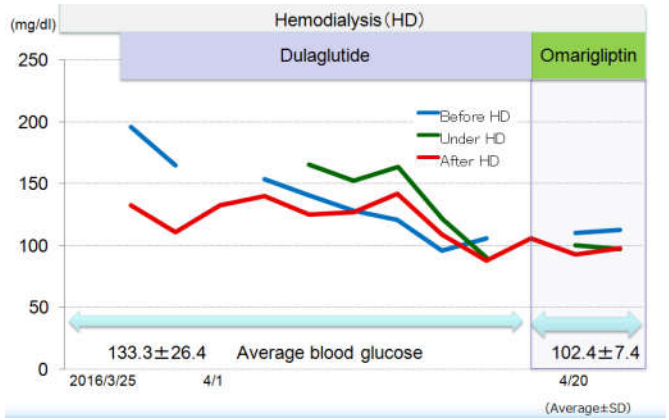

Figure 3.Case 3. 43 years old. Man Hemodialysis with type 2 diabetes

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 antidiabetic agents. Once-weekly oral medications may simplify the treatment regimen and improve compliance (Polonsky *et al*., 2011). In Septenber 2015, omarigliptin 12.5 and 25mg once-weekly tables were approved for the treatment of patients with type 2 diabetes in Japan as monotherapy or combination therapy with other antidiabetic agents (Burness, 2015). Oral omarigliptin was generally well-tolerated in patients with type 2 diabetes when administered as monotherapy or in combination with other antidiabeticagents (Sheu *et al*., 2015; NCT01703221. Omarigliptin (MK-3102) clinical trial-placebo and sitagliptin-controlled monotherapy study in Japanese patients with type 2 diabetes mellitus (MK-3102-020); NCT01703221. A study of the safety and efficacy of MK-3102 compared with inadequate glycemic control on metformin (MK-3102-016); NCT01841697. Study to evaluate the safety and efficacy of the addition of omarigliptin (MK-3102) compared with the addition of sitagliptin in participants with type 2 diabetes mellitus with inadequate glycemic control on metformin (MK-3102-026); NCT01704261. Addition of omarigliptin (MK-3102) to participants with type 2 diabetes mellitus who have inadequate glycemic control on combination therapy with glimeiride and metformin (MK-3102-022). Omarigliptin is a potent, reversible, competitive DPP-4 inhibitor, and its inhibition constant (Ki) is 0.8 nM(Biftu *et al*., 2014). 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 (Biftu *et al*., 2014). In a multicenter, phase Ⅲ 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 (Sheu *et al*., 2015). The increased postprandial 4-h weighed mean active GLP-1 level induced by omarigliptin was twice than that by placebo (Addy *et al*., 2013). 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 (Addy *et al*., 2013). 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 (Giorda *et al*., 2014). Glucose fluctuation of omarigliptin was 116.5±10.7 mg/dl, and of dulaglutide was 158.2±43.0 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 swithing 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. Omarigliptinmonotherapy was considered to be more effective, and we realize the combination therapy of dulaglutide plus omarigliptin is also potentially useful in clinical medicine.

REFERENCES

Addy, C., D.Tatosian, X.S.Hou *et al*. 2013. Pharmacokinetic and pharmacodynamics effects of multiple-dose administration of omarigliptin, a novel once-weekly dipeptidyl peptidase-4 (DPP-4) inhibitor, in obese subjects with and without type 2 diabetes mellitus. *Diabetes*, 62:287.

Biftu, T., R. Sinha-Roy, P. Chen *et al*. 2014. Omarigliptin: a novel long-acting DPP-4 inhibitor for once-weekly

treatment of type 2 diabetes. *J.Med.Chem*, 57: 3205-3213.

Burness. C.B. 2015. Omarigliptin: first global approval. *Drugs*, 75: 1947-1952.

Drucker, DJ. and MA. Nauck. 2006. The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. *Lancet*, 368: 1696-1705.

Giorda, C.B., E.Nada, B.Tartaglino. 2014. Pharmacokinetics, safety, and efficacy of DPP-4 inhibitors and GLP-1 receptor agonists in patients with type 2 diabetes mellitus and renal or hepatic impairment. A systematic review of the literature. *Endocrine*, 46: 406-419.

NCT01703221. A study of the safety and efficacy of MK-3102 compared with inadequate glycemic control on metformin (MK-3102-016).

NCT01703221. Omarigliptin (MK-3102) clinical trial-placebo and sitagliptin-controlled monotherapy study in Japanese patients with type 2 diabetes mellitus (MK-3102-020).

NCT01704261. Addition of omarigliptin (MK-3102) to participants with type 2 diabetes mellitus who have inadequate glycemic control on combination therapy with glimeiride and metformin (MK-3102-022).

NCT01841697. Study to evaluate the safety and efficacy of the addition of omarigliptin (MK-3102) compared with the addition of sitagliptin in participants with type 2 diabetes mellitus with inadequate glycemic control on metformin(MK-3102-026).

Polonsky WH, Fisher L, Hessler D, Bruhn D, Best JH. 2011. Patient perspectives on once-weekly medications for diabetes. *Diabetes ObesMetab*., 13: 144-149.

Sheu, W.H., I. Gantz, M. Chen *et al*. 2015. Safety and efficacy of omarigliptin (MK-3102), a novel once-weekly DPP-4 inhibitor for the treatment of patients with type 2 diabetes. *Diabetes Care*, 38: 2106-2114.

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