SUNTEXT REVIEWS

SunText Review of Pharmaceutical Sciences

ISSN: 2766-5232

Open Access

Case Report

Volume 5:1

Clinically Beneficial Effect for Elderly Type 2 Diabetes (T2D) by Combined Agents of Vildagliptin and Metformin as EquMet

Ikezoe M[1], Bando H[1,2,3,*], Kawahito A[1], Sueki E[1], Aihara A[1], Fujii F[1], Kanazawa S[1], Fukushima N[1] and Kato Y[1]

[1]*Kanaiso Hospital, Tokushima, Japan*

[2]*Japan Low Carbohydrate Diet Promotion Association, Kyoto, Japan*

[3]*Tokushima University / Medical Research, Tokushima, Japan*

[*]**Corresponding author:** Bando H, Tokushima University / Medical Research, Nakashowa 1-61, Tokushima, 770-0943, Japan; E-mail: pianomed@bronze.ocn.ne.jp

Received date: 05 September 2024; **Accepted date:** 13 September 2024; **Published date:** 20 September 2024

Citation: Ikezoe M, Bando H, Kawahito A, Sueki E, Aihara A, Fujii F, et al. (2024). Clinically Beneficial Effect for Elderly Type 2 Diabetes (T2D) by Combined Agents of Vildagliptin and Metformin as EquMet. SunText Rev Pharm Sci 5(1): 129.

DOI: https://doi.org/10.51737/2766-5232.2024.029

Copyright: © 2024 Ikezoe M, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

The case is 85-year-old female with Type 2 diabetes (T2D). She felt general malaise and thirsty in February 2024, and visited our clinic. Biochemistry showed HbA1c 9.2% for severe T2D. She was advised to start mild degree of petite low carbohydrate diet (LCD) and taking for a walk. For oral hypoglycemic agents (OHAs), she began vildagliptin (Equa) at first, followed by Metformin (Metgluco) with gradual increase of the doses, to EquMet LD. HbA1c decreased to 6.7% for 3 months, which was satisfactory without gastro-intestinal adverse effects (GI-AE). EquMet LD is expected for lower mean amplitude of glycemic excursions (MAGE).

Keywords: Petite low carbohydrate diet (Petite LCD); Vildagliptin/Metformin (EquMet); Mean amplitude of glucose excursions (MAGE); Japan LCD promotion Association (JLCDPA); Oral hypoglycemic agents (OHAs)

Introduction

Type 2 diabetes (T2D) has been observed for crucial medical problem across the world [1]. From international point of view, diabetic management has been in focus for many countries [2]. Considering the age group of people affected by diabetes, recent problem would be the adequate management for the elderly T2D cases. American Diabetes Association (ADA) has announced the standard measure for T2D in Jan 2024 [3]. It would be applied to the elderly T2D with applicable treatment using several types of oral hypoglycemic agents (OHAs). Among them, metformin has been the first-line agent for years and dipeptidyl peptidase-4 inhibitors (DPP-4i) has been used widely for its effectiveness. From these, the combined oral hypoglycemic agents (OHAs) have been used in the clinical practice. The combination of vildagliptin/metformin (EquMet) has been used with clinical effectiveness [4].

As to T2D, basic therapeutic principle would be nutrition therapy, exercise and OHAs or insulin. As diet therapy, calorie restriction (CR) method was previously standard, but low carbohydrate diet (LCD) has been evaluated for applicable measure [5]. LCD was initiated at first by the doctors of Atkins and Bernstein [6,7]. Successively, LCD was begun in Japan by our research group through the activities of Japan LCD promotion Association (JLCDPA) [8,9]. In addition, our team has developed LCD socially in Japan by seminars, books and medical societies [10]. We have announced useful three kinds of LCD diets for a variety of chances. They are petite-LCD, standard-LCD and super-LCD. It presents the ratio of including carbohydrate as 40%, 26% and 12%, respectively [11].

We have continued diabetic practice and research for years, and published lots of reports for various types of T2D and treatments [12,13]. Recently, we have an experience of meaningful T2D case. She was elderly female and showed significant effect by petite LCD and EquMet administration. Her clinical course and related perspectives will be described in this article.

Presentation of Cases

History and physicals

This case is 85-year-old female with T2D. As her past history, she was pointed out to have mild T2D about 4 years ago, and treated at another family physician. She had medical problems of T2D, mild hypertension, Gastro esophageal reflux disease (GERD) and has been stable for a few years. Recently, she cannot take medicine regularly for several months, and she visited our clinic in February 2024 associated with general malaise and thirsty.

The physical examination revealed in the following: conversation, consciousness and general movement were unremarkable. Vitals were pulse 80/min, BP 172/82, BT 36.8, respiration normal and SpO2 97%. Her head, lung, heart, abdomen and neurological findings were negative. Her physique showed height 150.4cm, weight 41.2 kg and BMI 18.2 kg/m^2. The chest X-ray showed negative, and electrocardiogram (ECG) showed within normal limits.

By rapid testing of HbA1c in the out-clinic, she was diagnosed as severe degree of T2D with HbA1c 9.2%. In addition, blood chemistry was conducted, and the results of liver, renal, lipids and complete blood count showed unremarkable (Table 1).

Clinical course and treatment

After she was currently judged as severe level of T2D, she was provided diabetic treatment for diet therapy, exercise, and pharmacotherapy. She was advised to start mild degree of petite low carbohydrate diet (LCD), and taking for a walk around her home for 30 minutes. For oral hypoglycemic agents (OHAs), she was advised to take vildagliptin (Equa) at first, followed by Metformin (Metgluco) with gradual increase of the doses. From May 2024, she was provided the combined agent of EquMet LD, which includes vildagliptin 50mg and metformin 250mg per tablet. Other medicines included amlodipine besilate 2.5mg, empagliflozin 10mg, miglitol 150 mg, and vonoprazan fumarate 10mg.

Concerning her clinical course, remarkable reduction of HbA1c was observed every month. HbA1c was decreased to 6.7% linearly until May 2024 with significant reduction for 3 months (Figure 1).

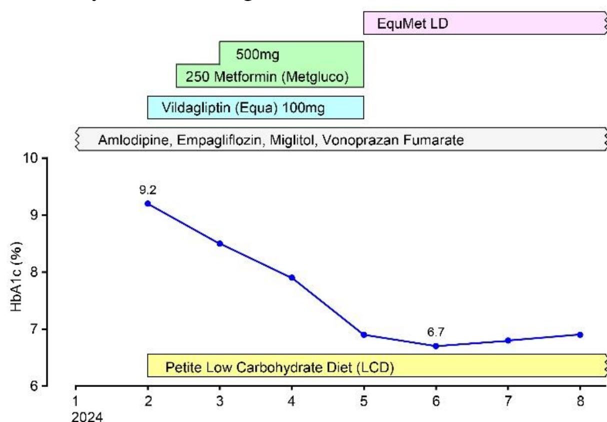

Table 1: *Changes in laboratory data.*

Figure 1: *Clinical course of the case with HbA1c and medication.*

	2024 Feb	2024 Aug	Units
Liver			
AST	32	17	(U/L)
ALT	25	14	(U/L)
GGT	15	13	(U/L)
Renal			
UA	2.8	3.5	(mg/dL)
BUN	13	14	(mg/dL)
Cre	0.72	0.78	(mg/dL)
Lipids			
HDL	51	64	(mg/dL)
LDL	121	125	(mg/dL)
TG	122	91	(mg/dL)
CBC			
WBC	76	74	(x10*2/μL)
RBC	374	369	(x10*4/μL)
Hb	12.9	12.6	(g/dL)
PLT	32.0	31.6	(x10*4/μL)

During her improving period, she did not complain of any symptoms for gastro-intestinal adverse effects (GI-AE). She can tolerate the treatment well, and no other clinical problems were found.

Ethical standards

This report was complied with the ethical guideline of Declaration of Helsinki [14]. Moreover, certain comment is with the protection regulation. The principle has been accompanied with ethic regulation for clinical practice and research. This guideline is observed in Japanese Ministry, including Ministry of Education, Culture, Sports, Science Technology and Ministry of Health, Labor and Welfare in Japan.

The authors and collaborators have set the ethical committee in the hospital. It has hospital director, doctors, nurse, pharmacist, and legal professional. These members discussed fully the protocol and agreed. The informed consent was given from the case with the document.

Discussion

This case is 85-year-old case with T2D, who showed remarkable improvement of glucose variability for a few months. She is elderly patient with T2D, hypertension and GERD, without apparent high degree of arteriosclerosis, because she did not have distinct macroangiopathy, such as cerebrovascular accident (CVA), ischemic heart disease (IHD), or peripheral artery disease (PAD). During her clinical course, her body weight has been stable. It would be because the muscle volume did not change so much, irrespective of the improvement of glucose variability.

Concerning the remarkable effectiveness, another reason may be considered. This elderly case has applied petite LCD, in which she

did not change the meal pattern so much. She continued to eat less carbohydrate amount than before, and then she always ate some rice or carbohydrate in the supper. Among some types of DPP4-i, Equa or EquMet shows the characteristic point, which is administering twice a day. From this benefit, vildagliptin can suppress the fluctuation of blood glucose for all day. In other words, she possibly obtained smaller mean amplitude of glycemic excursions (MAGE) than before [15]. When vildagliptin is given at night, glucose elevation can be reduced during midnight. This mechanism may bring the significant improvement of glucose variability in this case.

As regards to macroangiopathy in T2D, protection of the exacerbation of arteriosclerosis would be considered. Earlier administration of combined vildagliptin/metformin (EquMet) showed the satisfactory reduction of risk for macrovascular events [4,16]. It was the sub-analysis of investigations of VERIFY, which stands for vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY) [4,16]. Among VERIFY exams, two categories were compared for young and late-onset T2D. As the protocol, end point was set for the treatment failure (TF) that means the elevation of HbA1c as 7.0%. As a result, the risk was calculated as 46% vs 48% for late-onset cases vs young-onset cases with significant difference [17]. Consequently, treatment-naïve young cases showed the improvement of early durability and later exacerbation for glycemic variability.

Petite LCD was applied for this case, which seemed to be beneficial and satisfactory. From historical point of view in medical region, the comparison of CR, LCD and Mediterranean Diet (MD) was conducted by Shai et al [18]. LCD was proved to be effective for almost cases in short period, but the rebound phenomenon has been often observed [19]. Then, the compromised method has been found for the combined therapy of LCD and MD, where LCD would be started at first, followed by MD several months later [5]. In addition, MD and Paleolithic diet have been compared for beneficial measure [20]. Future interests may attract attention for MD, LCD and prevention of CVD [21,22].

Authors and co-researchers have presented diabetic reports [23]. Among them, seasonal changes of HbA1c with EquMet for 6 years was included [24]. We will continue diabetic research with various points of view [25].

Some limitation may be found in this report. This is only one case, and she showed significant improvement by petite LCD and EquMet. She did not have currently apparent diabetic macroangiopathy, but we should pay attention to the exacerbation of complication. Diabetic strategy is to minimize the aggravation of Atherosclerotic Cardiovascular Disease (ASCVD) for the clinical progress.

In summary, 85-year-old female was presented with some perspectives. Clinical course will be followed up with careful attention for preventing development of arteriosclerosis. We expect that this article will become useful reference for diabetic practice.

Conflict of Interest

The authors declare no conflict of interest.

Funding

There was no funding received for this paper.

References

1. Reurean-Pintilei D, Potcovaru CG, Salmen T, Mititelu-Tartau L, Cinteză D, Lazăr S, et al. Assessment of Cardiovascular Risk Categories and Achievement of Therapeutic Targets in European Patients with Type 2 Diabetes. J Clinical Med. 2024; 13: 2196.
2. Rickenbach A, Acheampong MK, Bogar A, Booth G. Perspectives of the World Health Organization's physical activity guidelines among patients with musculoskeletal conditions: A mixed-methods survey. Musculoskeletal Care. 2024; 22: e1868.
3. American Diabetes Association Professional Practice Committee; 1. Improving Care and Promoting Health in Populations: Standards of Care in Diabetes- 2024. Diabetes Care. 2024; 47: S11-S19.
4. Matthews DR, Palda´nius PM, Proot P, Chiang Y, Stumvoll M, Del Prato S. Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial. Lancet. 2019; 394: 1519-1529.
5. Currenti W, Losavio F, Quiete S, Alanazi AM, Messina G, Polito R, et al. Comparative Evaluation of a Low-Carbohydrate Diet and a Mediterranean Diet in Overweight/Obese Patients with Type 2 Diabetes Mellitus: A 16-Week Intervention Study. Nutrients. 2023; 16: 95.
6. Atkins and Robert. Dr. Atkins' New Carbohydrate Gram Counter. M. Evans and Company. 1996.
7. Bernstein RK. Dr. Bernstein's Diabetes Solution. Little, Brown and company, New York. 1997.
8. Ebe K, Wood M, Bando H. Preventing Post-Prandial Elevation of Blood Glucose by Breakfast with Less Carbohydrate. Int J Case Rep Clin Image 2024; 6: 219.
9. Muneta T, Hayashi M, Nagai Y, Matsumoto M, Bando H, et al. Ketone Bodies in the Fetus and Newborn During Gestational Diabetes and Normal Delivery. Int J Diabetes. 2023; 5: 157-163.
10. Wood M, Ebe K, Bando H. Role of Low-Carbohydrate Diets in Diabetes Management. SunText Rev Endocrine Care. 2024; 3: 118.
11. Bando H, Ebe K. Beneficial and Convenient Method of Low Carbohydrate Diet (LCD) as Petite, Standard and Super LCD. Asp Biomed Clin Case Rep. 2023; 7: 1-4.
12. Arakawa T, Bando H, Ogawa H, Nagahiro S, Nakanishi M, Watanabe O. Clinical Improvement by Vildagliptin/Metformin (Equmet) For Diabetic Patient with Remarkable Arteriosclerosis from Slight Hba1c Elevation for Years. Int J Case Rep Clin Image. 2023; 5: 206.

13. Bando H, Okada M, Iwatsuki N, Ogawa T, Sakamoto K. Parallel Improvement of Hba1c and Arteriosclerosis during Clinical Progress for Diabetic Patient. SunText Rev Endocrine Care. 2024; 4: 121.
14. General Assembly of the World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. J Am Coll Dent. 2014; 81: 14-18.
15. Marfella R, Barbieri M, Grella R, Rizzo MR, Nicoletti GF, Paolisso G. Effects of vildagliptin twice daily vs. sitagliptin once daily on 24-hour acute glucose fluctuations. J Diabetes Complications. 2010; 24: 79-83.
16. Matthews DR, Palda´nius PM, Stumvoll M. A pre-specified statistical analysis plan for the VERIFY study: Vildagliptin efficacy in combination with metformin for early treatment of T2DM. Diabetes. Obes Metab. 2019; 21: 2240-2247.
17. Chan JCN, Paldánius PM, Mathieu C, Stumvoll M, Matthews DR, Del Prato S. Early combination therapy delayed treatment escalation in newly diagnosed young-onset type 2 diabetes: A subanalysis of the VERIFY study. Diabetes Obes Metab. 2021; 23: 245-251.
18. Shai I. Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med. 2008; 359: 229-241.
19. Pavlidou E, Papadopoulou SK, Fasoulas A, Mantzorou M, Giaginis C. Clinical Evidence of Low-Carbohydrate Diets against Obesity and Diabetes Mellitus. Metabolites. 2023; 13: 240.
20. Zamani B, Zeinalabedini M, Nasli Esfahani E, Azadbakht L. Can Following Paleolithic and Mediterranean Diets Reduce the Risk of Stress, Anxiety, and Depression: A Cross-Sectional Study on Iranian Women. J Nutr Metab. 2023; 2023: 2226104.
21. Hareer LW, Lau YY, Mole F, Reidlinger DP, O'Neill HM, Mayr HL, Greenwood H, Albarqouni L. The effectiveness of the Mediterranean Diet for primary and secondary prevention of cardiovascular disease: An umbrella review. Nutr Diet. 2024.
22. Zheng X, Zhang W, Wan X, Lv X, Lin P, Si S, Xue F, Wang A, Cao Y. The effects of Mediterranean diet on cardiovascular risk factors, glycemic control and weight loss in patients with type 2 diabetes: a meta-analysis. BMC Nutr. 2024; 10: 59.
23. Okada M, Bando H, Iwatsuki N, Ogawa T, Sakamoto K. Diabetic patient with arteriosclerosis and cholelithiasis treated by imeglimin (Twymeeg) and vildagliptin/metformin (EquMet).Int J Endocrinol Diabetes. 2023; 6: 154.
24. Bando H, Yamashita H, Kato Y, Kawata T, Kato Y, Kanagawa H. Seasonal Variation of Glucose Variability in Rather Elderly Patients with Type 2 Diabetes (T2D) Treated by Vildagliptin and Metformin (EquMet). Asp Biomed Clin Case Rep. 2022; 5: 146-151.
25. Ogawa T, Bando H, Iwatsuki N, Okada M, Sakamoto K. Remarkable Effects for HbA1c and Weight by Twymeeg (imeglimin) and EquMet in Type 2 Diabetes (T2D) Patient. SunText Rev Endocrine Care. 2024; 4: 120.