Asploro Journal of Biomedical and Clinical Case Reports
(ISSN: 2582-0370)
Case Report
DOI: https://doi.org/10.36502/2026/ASJBCCR.6443

Improvement of HbA1c and LDL-C by Imeglimin (Twymeeg) in the Diabetic Female Elderly

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Received date: 9 April 2026; **Accepted date**: 11 May 2026; **Published date**: 18 May 2026

Citation: Ogawa T, Bando H, Iwatsuki N, Okada M, Sakamoto K. Improvement of HbA1c and LDL-C by Imeglimin (Twymeeg) in the Diabetic Female Elderly. Asp Biomed Clin Case Rep. 2026 May 18;9(2):66-70.

Abstract

The case is a 77-year-old female who was treated for arteriosclerosis and gastroesophageal reflux disease (GERD). In March 2025, type 2 diabetes (T2D) was detected, with HbA1c of 8.8%. Physical examination was negative, with BMI of 21.7 kg/m^2. Blood chemistry examination revealed LDL of 142 mg/dL, and pulse wave velocity (PWV) showed a cardio-ankle vascular index (CAVI) of 9.9/9.6 and ankle-brachial index (ABI) of 1.11/1.07.

She was advised to follow a petite low-carbohydrate diet (LCD), treated with imeglimin (Twymeeg), and subsequently received rosuvastatin, vildagliptin, and metformin. As a result, she showed improvement, with HbA1c of 7.0% and LDL of 78 mg/dL in March 2026, indicating remarkable clinical efficacy.

Keywords

Petite Low-Carbohydrate Diet, Pulse Wave Velocity, Japan LCD Promotion Association, Oral Hypoglycemic Agent, Trials of IMeglimin for Efficacy and Safety

Abbreviations

LCD: Low-Carbohydrate Diet; PWV: Pulse Wave Velocity; JLCDPA: Japan LCD Promotion Association; OHA: Oral Hypoglycemic Agent; TIMES: Trials Of IMeglimin For Efficacy And Safety; T2D: Type 2 Diabetes; GERD: Gastroesophageal Reflux Disease; CAVI: Cardio-Ankle Vascular Index; ABI: Ankle-Brachial Index.

Introduction

Recently, older people have faced clinical problems related to diabetes, non-communicable diseases (NCDs), and arteriosclerotic cardiovascular diseases (ASCVDs) worldwide [1]. Among them, fundamental nutritional treatment and adequate medication are required [2]. The authors have continued clinical practice for NCDs and ASCVDs and published various reports [3].

Concerning diet therapy, calorie restriction (CR) was formerly well known. After that, Dr. Bernstein proposed the clinical efficacy of the low-carbohydrate diet (LCD) in the medical and healthcare fields [4]. In Japan, the authors' group established the Japan LCD Promotion Association (JLCDPA) and developed social

and clinical movements promoting LCD [5]. We proposed three practical and useful LCD methods: petite, standard, and super LCD, in which the carbohydrate ratios are 40%, 26%, and 12%, respectively [6]. By applying these approaches, clinical improvement in T2D has been observed [7].

For diabetic pharmacology, imeglimin (Twymeeg) has been introduced into medical practice as a novel oral hypoglycemic agent (OHA) [8]. It shows benefits when combined with other OHAs [9]. It has a unique mechanism that increases insulin secretion from beta cells and decreases insulin resistance [10,11]. As a matter of fact, imeglimin has been reported to provide clinical efficacy for T2D cases with comorbidities and complications [12]. During our clinical practice, we encountered an impressive female patient with T2D and dyslipidemia treated with imeglimin (Twymeeg). Her general clinical progress, with related discussion, is described in this article.

Case Report

History and Physical Examination:

This case involved a 77-year-old female who was diagnosed with arteriosclerosis and gastroesophageal reflux disease (GERD) by the Department of Neurosurgery. She had no obvious symptoms or signs, but had been prescribed Lixiana and lansoprazole. In March 2025, hyperglycemia was incidentally detected, and she was referred to the diabetic department for further evaluation.

Physical examination revealed no abnormalities in vital signs, level of consciousness, head, neck, chest, abdomen, or neurological examination. Her physique measurements were 151.2 cm in height, 49.7 kg in weight, and BMI 21.7 kg/m^2.

Several Examinations:

As basic tests, urinalysis, chest X-ray, and electrocardiogram (ECG) showed no particular abnormalities. Blood biochemistry revealed elevated values of HbA1c 8.8%, blood glucose 202 mg/dL, and LDL 142 mg/dL, with unremarkable results for liver function, renal function, and complete blood count (CBC) (**Fig-1**).

	Units	2025 Mar	Apr	May	Sept	Oct	2026 Jan	Mar
Diabetes								
Treatment		imeglimin						
				vildagliptin, metformin				
HbA1c	(%)	8.8	8.1	7.7	7.5	7.2	7.3	7.0
glucose	(mg/dL)	202	168	208	251	133	139	139
Lipids								
Treatment			rosuvastatin					
LDL	(mg/dL)	142			76			78
HDL	(mg/dL)	73			56			71
TG	(mg/dL)	147			151			152
Nutrition								
TP	(g/dL)	7.3			6.8			7.4
Alb	(g/dL)	4.4			4.1			4.5
Liver								
AST	(U/L)	19			19			25
ALT	(U/L)	17			20			28
GGT	(U/L)	14			14			15
Renal								
UA	(mg/dL)	3.5			3.1			3.1
BUN	(mg/dL)	17			18			19
Cre	(mg/dL)	0.63			0.70			0.72
eGFR	(mL/min/1.73m^2)	69			61			59
CBC								
WBC	(x10^2/μL)	37			34			35
RBC	(x10^4/μL)	497			437			466
Hb	(g/dL)	14.9			13.2			14.4
Ht	(%)	46.1			41.1			44.7
Plt	(x10^4/μL)	17.9			17.1			19.5

Fig-1: Changes in Blood Chemistry and Treatment

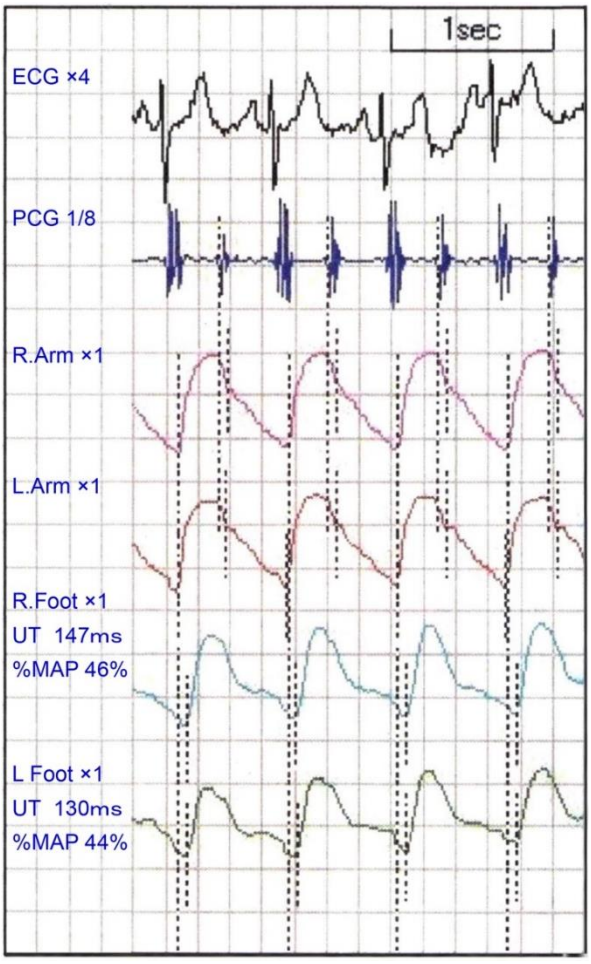

Fig-2: The Exam of Pulse Wave Velocity (PWV)

Pulse wave velocity (PWV) showed a cardio-ankle vascular index (CAVI) of 9.9/9.6 (R/L; normal 9.3 ± 0.9) and an ankle-brachial index (ABI) of 1.11/1.07 (normal range 0.91–1.40), respectively (**Fig-2**). Detailed biomarkers were normal: L(115) = L1(59) + L2(31) + L3(25), PEP 97, ET 302, R-AI 1.11, and PEP/ET 0.27.

MRI showed mild brain atrophy and ventricular enlargement, which were compatible with age. MRA showed mild signal reduction at the origins of the bilateral internal carotid arteries (**Fig-3**).

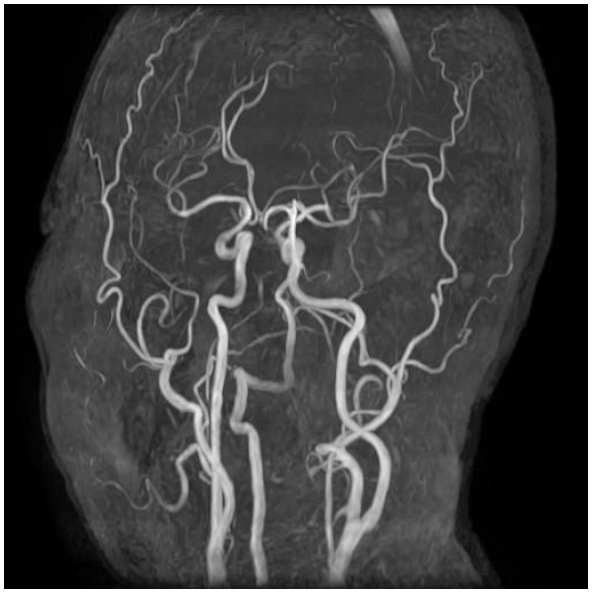

Fig-3: The finding of Brain MRI

Clinical Course:

The patient was diagnosed with T2D, and petite-LCD was initiated. For OHA treatment, imeglimin (Twymeeg) 2000 mg/day was started in March (**Fig-1**). From April, rosuvastatin 2.5 mg/day was initiated for dyslipidemia treatment. HbA1c gradually decreased, and vildagliptin and metformin were added from May 2025. Subsequently, HbA1c and LDL decreased to 7.0% and 78 mg/dL, respectively, over 12 months.

Ethical Standards:

This case complied with the guidelines of the Declaration of Helsinki. Commentary was added regarding personal information in accordance with ethical principles for clinical research. The required guidelines were based on regulations from the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare.

The authors established an ethics committee at Sakamoto Hospital, including the director, physicians, a nurse, a nutritionist, a pharmacist, and a legal professional. The protocol was discussed and approved, and informed consent was obtained from the patient.

Discussion

This case had several characteristic features:

#1 She had no particular symptoms, signs, or episodes suggestive of T2D;

#2 BMI was normal without overweight;

#3 HbA1c decreased from 8.8% to 7.7% within two months by imeglimin (Twymeeg);

#4 Further HbA1c reduction was observed after adding vildagliptin and metformin;

#5 LCD was mild in degree, with ordinary breakfast and supper intake;

#6 Arteriosclerosis was not apparent in the brain, heart, or extremities.

The first-line use of imeglimin appeared useful. She continued petite-LCD while eating ordinary breakfast and supper. Imeglimin is administered twice daily (bis in die, BID). International multicenter studies, Trials of IMeglimin for Efficacy and Safety (TIMES) 1, 2, and 3, have been conducted. Among them, TIMES 1 compared administration of 1000 mg BID and placebo [13]. Comparisons of 1000 mg and 1500 mg BID were also performed [14]. Long-term administration of imeglimin has demonstrated clinical efficacy in various situations [15].

The current case received combined therapy with imeglimin, vildagliptin, and metformin. According to the TIMES results, HbA1c reduction effects for combined OHAs were 0.46% in monotherapy, 0.67% with biguanides, 0.92% with DPP4-i, and 0.57% with SGLT2-i. Combined OHAs may therefore have contributed to the enhanced clinical benefit observed in this case [16].

As part of her clinical course, combined therapy with vildagliptin and metformin (EquMet) was added.

HbA1c gradually improved, although she continued consuming carbohydrates at breakfast and supper. EquMet is characterized by BID administration and hypoglycemic efficacy during nighttime [17]. Regarding glucose variability, vildagliptin BID can decrease the mean amplitude of glycemic excursions (MAGE) compared with sitagliptin [18]. These findings suggest that the combined OHAs suppressed postprandial hyperglycemia during nighttime.

Treatment of diabetes also requires management of dyslipidemia. This case initiated dyslipidemia treatment simultaneously with OHA therapy for diabetes [19]. According to the Standards of Care in Diabetes-2026, "In diabetic elderly patients aged >75 years, it may be reasonable to initiate moderate-intensity statin therapy after evaluating and discussing the potential benefits and risks (Level C)" [20]. In this case, LDL levels decreased sufficiently with rosuvastatin treatment. This may be because she had no previous medication history and was receiving pharmacological treatment for the first time [21].

Certain limitations may exist in this report. The current case involved several specific issues, including T2D, dyslipidemia, imeglimin, vildagliptin, and related factors. Her arteriosclerosis appeared to remain within an almost standard range, and her clinical course should continue to be followed carefully.

In summary, a 77-year-old female was presented with related clinical perspectives. This description may be useful for future clinical practice and research concerning diabetes and arteriosclerosis in the aging society.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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