

Received: 2016.07.15
Accepted: 2016.08.31
Published: 2016.11.25

Postprandial and Orthostatic Hypotension Treated by Sitagliptin in a Patient with Dementia with Lewy Bodies

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Conflict of interest: None declared

Patient: Female, 78
Final Diagnosis: Dementia with Lewy body
Symptoms: Dizziness • syncope
Medication: —
Clinical Procedure: —
Specialty: Geriatrics

Objective: Unusual setting of medical care

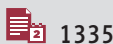
Background: Postprandial hypotension, induced by an absorption of glucose from intestine, could be treated by acarbose; however, it was unclear whether dipeptidyl peptidase-4 inhibitor reduced postprandial hypotension.

Case Report: A 78-year-old woman who had experienced episodes of dizziness and hypotension after eating was admitted to our hospital. During 24-hour ambulatory blood pressure monitoring, there were repeated episodes of marked postprandial hypotension; i.e., a significant systolic blood pressure reduction within two hours after eating (from -58 to -64 mm Hg after meals). The patient was diagnosed with dementia with Lewy bodies. The patient exhibited postprandial hyperglycemia and hypotension after a 75 g oral glucose tolerance test. After the administration of 25 mg sitagliptin, the patient's postprandial and orthostatic hypotension was reduced remarkably. Moreover, her Mini-Mental State Examination score subsequently increased (from 22 to 25 points).

Conclusions: The dipeptidyl peptidase-4 inhibitor sitagliptin can delay postprandial increases in glucose levels and hypotensive episodes, as well as sympathetic nervous system abnormalities and orthostatic hypotension.

MeSH Keywords: Autonomic Nervous System Diseases • Hypotension • Hypotension, Orthostatic • Lewy Body Disease • Postprandial Period

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/900620>



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Background

Postprandial hypotension and orthostatic hypotension can cause syncope and falls in elderly patients, leading to cognitive decline and a reduction in quality of life. One of the causes of postprandial hypotension is carbohydrate ingestion. Carbohydrates in the intestine increase mesenteric arterial blood flow and reduce systemic venous flow, which leads to reductions in cardiac output and systemic blood pressure. In patients with autonomic nervous system dysfunction, delayed systemic blood pressure responses to increased mesenteric arterial flow can cause postprandial hypotension, and α -glucosidase inhibitors such as acarbose have been reported to improve postprandial hypotension [1]. In a recent case report, it was reported that dipeptidyl peptidase-4 (DPP-4) inhibitors can also ameliorate postprandial hypotension [2]. However, there have not been any reports about the relationship between postprandial glucose levels before and after the administration of DPP-4 inhibitors in patients with autonomic nervous system dysfunction due to dementia with Lewy bodies. Moreover, it is unclear whether DPP-4 inhibitors improve orthostatic hypotension and/or postprandial hypotension.

Case Report

A 78-year-old woman, who was suffering from dizziness after meals, was admitted to our hospital. The patient had a previous history of hypertension and ischemic stroke (from the right external capsule to the putamen) six months earlier, and after her stroke, she had dizziness and faintness after meals and also experienced postprandial systolic blood pressure reductions (from 130 mm Hg to 80 mm Hg). Her family felt that she was suffering from cognitive impairment. The patient was referred to our hospital to have her postprandial hypotension evaluated and managed.

No abnormalities were observed during her physical examinations. The findings of her blood examinations are shown in Table 1. Cardiomegaly was not observed on a chest x-ray, and an electrocardiogram showed a normal sinus rhythm. No significant stenosis was detected in the carotid arteries on echosonography.

The results of the patient's 24-hour ambulatory blood pressure monitoring are shown in Figure 1. The patient's systolic blood pressure dropped from 143 mm Hg to 77 mm Hg at 30 minutes after meals, which was suggestive of marked postprandial hypotension. She also exhibited orthostatic hypotension (a reduction in systolic blood pressure from 160 mm Hg to 120 mm Hg) in the head-up tilt test (Figure 2). In an evaluation of the patient's heart rate variability during standing up and sitting down (Kiritsu Meijin, Crosswell Inc., Kanagawa, Japan), a reduced sympathetic nervous system activity response, which

Table 1. Characteristics and blood examination of the patient.

Age, 78, years
Gender, Female
Body height, 151 cm
Body weight, 54 kg
Body mass index, 23.7 kg/m ²
White blood cells, 5,680 (4,000–7,500)/ μ L
Hemoglobin, 12.7 (11.5–15.5) g/dL
Platelet, 14.5 \times 10 ³ (12.0–34.0 \times 10 ³)/ μ L
Fasting blood glucose, 125 (65–110), mg/dL
Hemoglobin A1c, 6.0 (4.6–6.2) %
Total bilirubin, 0.9 (0.2–1.0), mg/dL
Aspartate aminotransferase (AST), 18 (8–38) IU/L
Alanine aminotransferase (ALT), 11 (4–44) IU/L
Lactate dehydrogenase (LD), 159 (106–211) IU/L
Creatinine phosphokinase, 67 (14–180) IU/L
Blood urea nitrogen, 15.0 (10–25) mg/dL
Creatinine, 1.08 (0.60–1.00) mg/dL
Na, 142 (138–146) mEq/L
K, 4.5 (3.5–4.7), mEq/L
Cl, 105 (97–110) mEq/L
C-reactive protein, 0.12 (<0.31) mg/dL

Data in the parenthesis shows normal values.

was measured as the change in the low frequency (LF)/high frequency (HF) power ratio observed after standing up, was detected (Table 2). In metaiodobenzylguanidine (MIBG) scintigraphy, a reduced heart-to-mediastinum uptake ratio (H/M ratio) was observed (1.77 on early images and 1.09 on delayed images), which was indicative of reduced sympathetic nervous function in the heart (Figure 3). In addition, the patient's Mini-Mental State Examination (MMSE) score was 22 points, and she was considered to be suffering from cognitive impairment without Parkinsonism. The patient was diagnosed with dementia with Lewy bodies based on the following findings: (1) rapid eye movement sleep behavior disorder, (2) autonomic nervous system dysfunction, (3) a reduced H/M ratio on MIBG scintigraphy, and (4) an abnormal pattern on a dopamine transporter (DAT) scan (Figure 4).

The results obtained by continuous blood pressure monitoring (Arteriograph24, TensioMed, Hungary) during the 75 g oral glucose ingestion test are shown in Table 3. The patient exhibited a blood pressure reduction at 30 minutes after the ingestion of 75 g oral glucose, which was not affected by her serum insulin levels, and she also displayed postprandial hyperglycemia. On the other hand, the patient did not demonstrate a

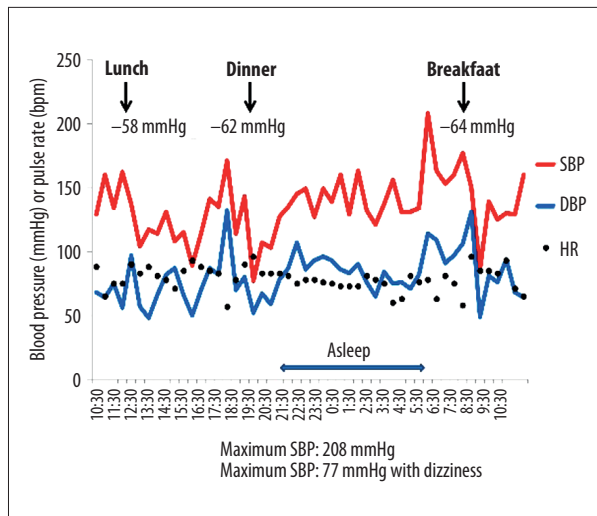


Figure 1. 24-hour ambulatory blood pressure monitoring before the administration of sitagliptin. Ambulatory blood pressure monitoring was performed at 15-minute intervals for 24 hours.

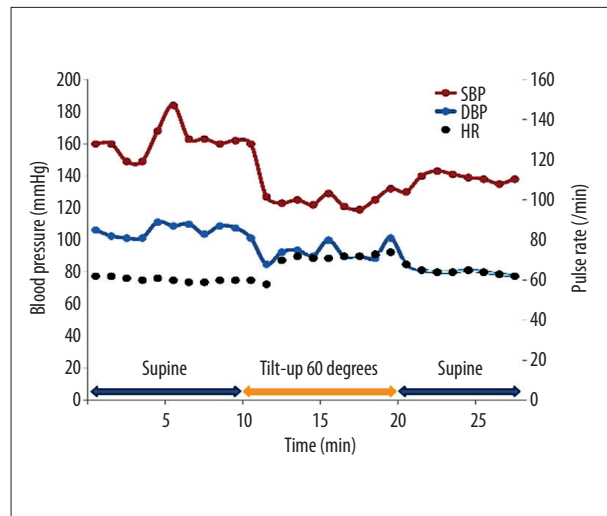


Figure 2. Head-up tilt test results obtained before the administration of sitagliptin. Blood pressure was measured using an automatic cuff-oscillometric device at 5-minute intervals.

Table 2. Changes in heart rate variability measures after standing-up.

	Rest	Standing-up	Standing	Sitting-down
Baseline				
Systolic blood pressure, mmHg	147	116	106	131
Diastolic blood pressure, mmHg	81	67	69	81
Heart rate, bpm	62	66	69	69
High frequency (HF), Hz	134.59	137.03	55.92	46.65
Low frequency (LF), Hz	124.57	111.52	57.01	63.06
LF/HF ratio	1.26	0.83	1.22	1.72
After taking sitagliptin 25 mg just after waking up				
Systolic blood pressure, mmHg	140	127	130	126
Diastolic blood pressure, mmHg	79	80	77	77
Heart rate, bpm	74	77	76	74
High frequency (HF), Hz	38.73	39.20	18.35	51.40
Low frequency (LF), Hz	30.28	41.11	27.53	99.77
LF/HF ratio	0.81	1.02	1.66	2.04

reduction in blood pressure after the intravenous administration of 20 mL 20% glucose (Table 3), which suggested that the absorption of glucose from the intestine, rather than glucose in the blood, played an important role in the causative mechanism of the patient's postprandial hypotension.

The patient was prescribed 25 mg of the DPP-4 inhibitor sitagliptin to be taken just after she woke. During her subsequent

24-hour ambulatory blood pressure monitoring (Figure 5), it was found that the magnitude of her postprandial hypotension had reduced, especially after breakfast (-33 mm Hg) and after lunch (-33 mm Hg). Furthermore, her postprandial blood pressure did not fall below 100 mm Hg, and she did not complain of dizziness. In addition, the patient did not exhibit orthostatic hypotension during the head-up tilt test (Figure 6). In the 75 g oral glucose ingestion test, no blood pressure reduction

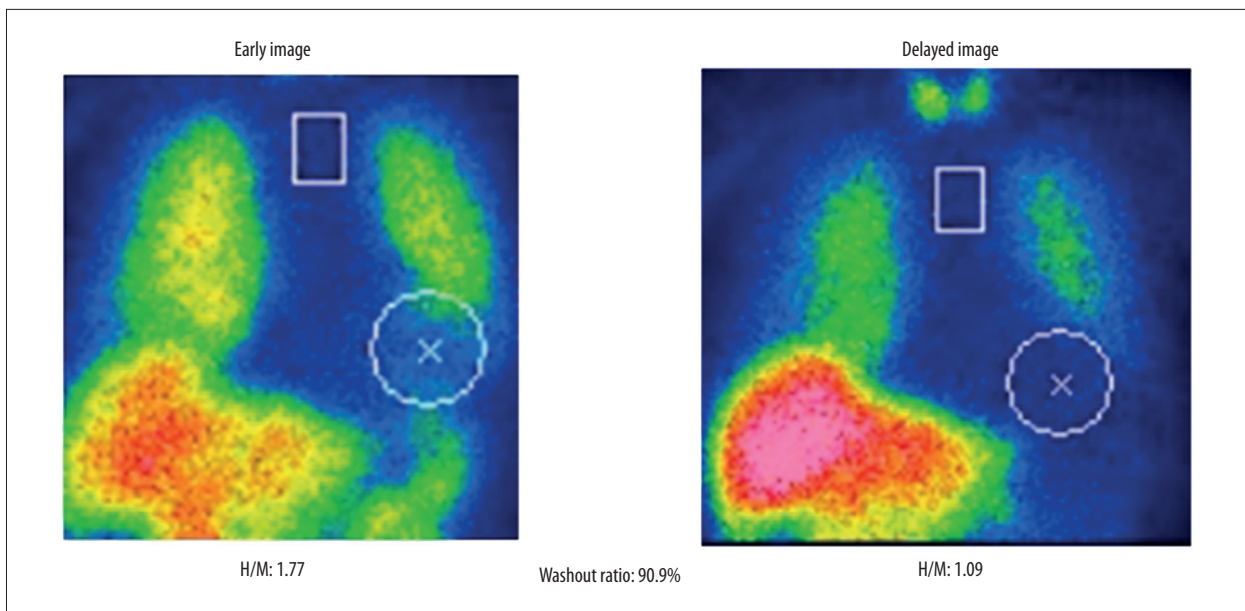


Figure 3. H/M ratio on MIBG scintigraphy before the administration of sitagliptin.

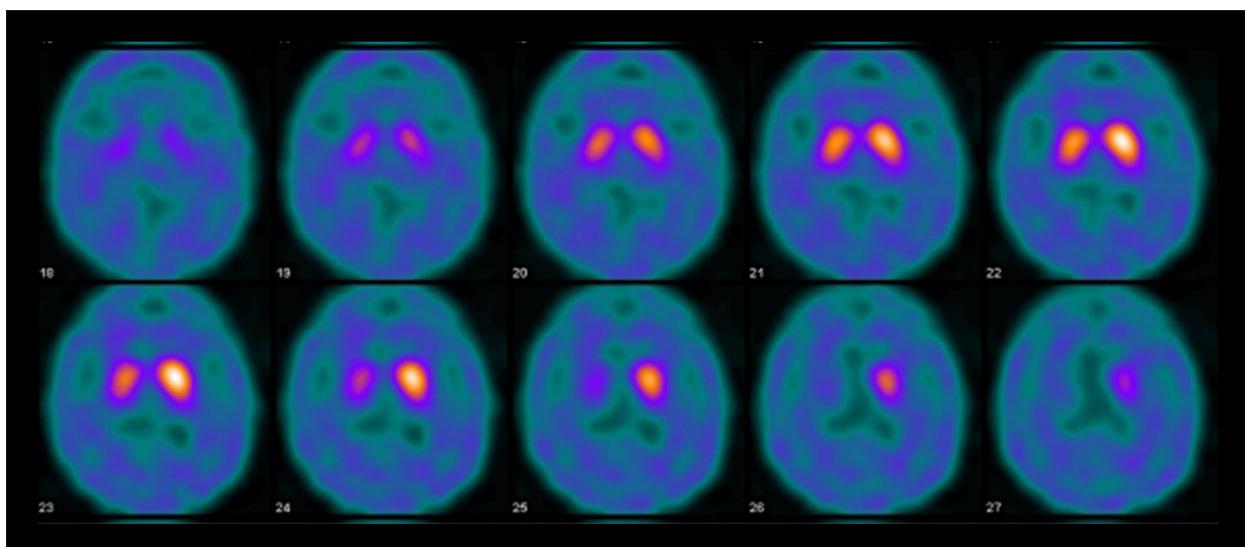


Figure 4. The patient's DAT scans.

was seen after the ingestion of glucose (Table 3). In a heart rate variability analysis performed during standing up and sitting down, an improvement in sympathetic nervous system activation; i.e., the change in the LF/HF ratio observed after standing up, was detected (Table 2). However, the H/M ratio detected on MIBG scintigraphy did not change after the patient started taking sitagliptin (Figure 7). After the patient's postprandial and orthostatic hypotensive episodes ceased, her cognitive impairment; i.e., her MMSE score, improved (22 points to 25 points).

Even after one year of initiation of sitagliptin, the patient did not experience faintness or dizziness after meals. During her

24-hour ambulatory blood pressure monitoring, her postprandial hypotension reduced remarkably (Figure 8). Additionally, the patient did not have any hypoglycemic episodes during the follow-up period.

Discussion

We experienced a case in which the patient exhibited postprandial and orthostatic hypotension due to autonomic nervous system dysfunction associated with dementia with Lewy bodies. In this patient, the ingestion of glucose that led to postprandial hypotension was found to play an important role in the

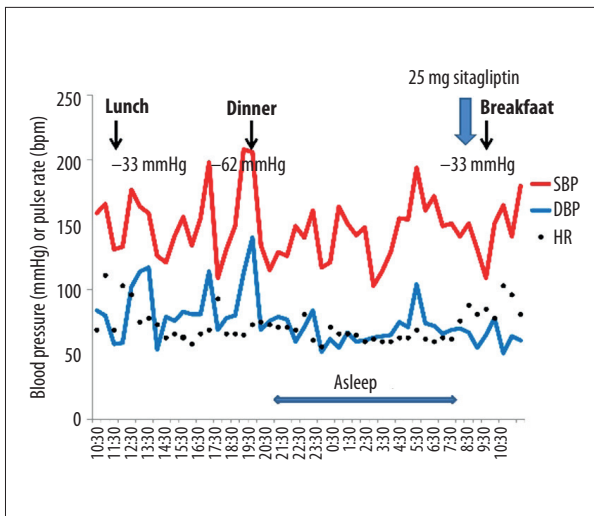


Figure 5. 24-hour ambulatory blood pressure monitoring after the administration of sitagliptin. Ambulatory blood pressure monitoring was performed at 15-minute intervals for 24 hours.

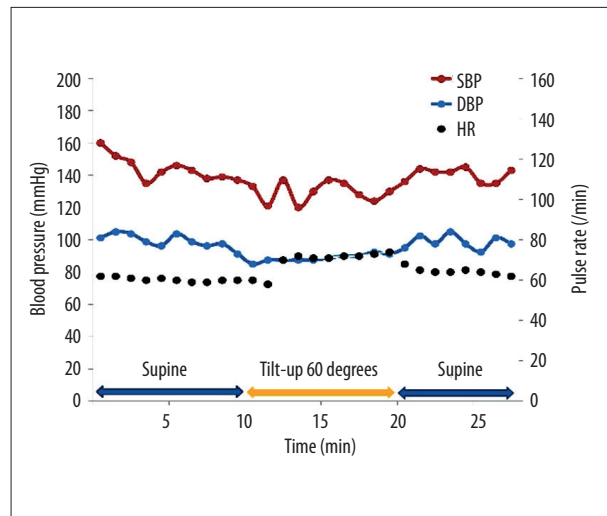


Figure 6. Head-up tilt test results obtained after the administration of sitagliptin. Blood pressure was measured using an automatic cuff-oscillometric device at 5-minute intervals.

Table 3. Changes in blood pressure, blood glucose, and insulin level after 75 g oral glucose ingestion or intravenous administration of 20% glucose 20 mL.

	Before	30 min	60 min	90 min	120 min
Baseline					
75 g oral glucose ingestion					
Systolic blood pressure, mm Hg	162	116	119	129	130
Diastolic blood pressure, mm Hg	90	69	72	80	80
Blood glucose, mg/dL	100	208	240	285	274
Insulin, μ U/L	4.4	19.2	25.8	36.3	58.5
20% glucose 20 mL intravenously					
Systolic blood pressure, mm Hg	146	147	157	176	160
Diastolic blood pressure, mm Hg	85	88	91	97	96
Blood glucose, mg/dl	100	120	106	102	103
Insulin, μ U/l	4.0	5.7	3.8	3.5	3.0
After taking sitagliptin 25 mg just after waking					
75 g oral glucose ingestion					
Systolic blood pressure, mm Hg	190	148	155	137	144
Diastolic blood pressure, mm Hg	103	80	85	81	84
Blood glucose, mg/dL	100	157	144	170	186
Insulin, μ U/L	4.5	20.7	13.7	18	23.8

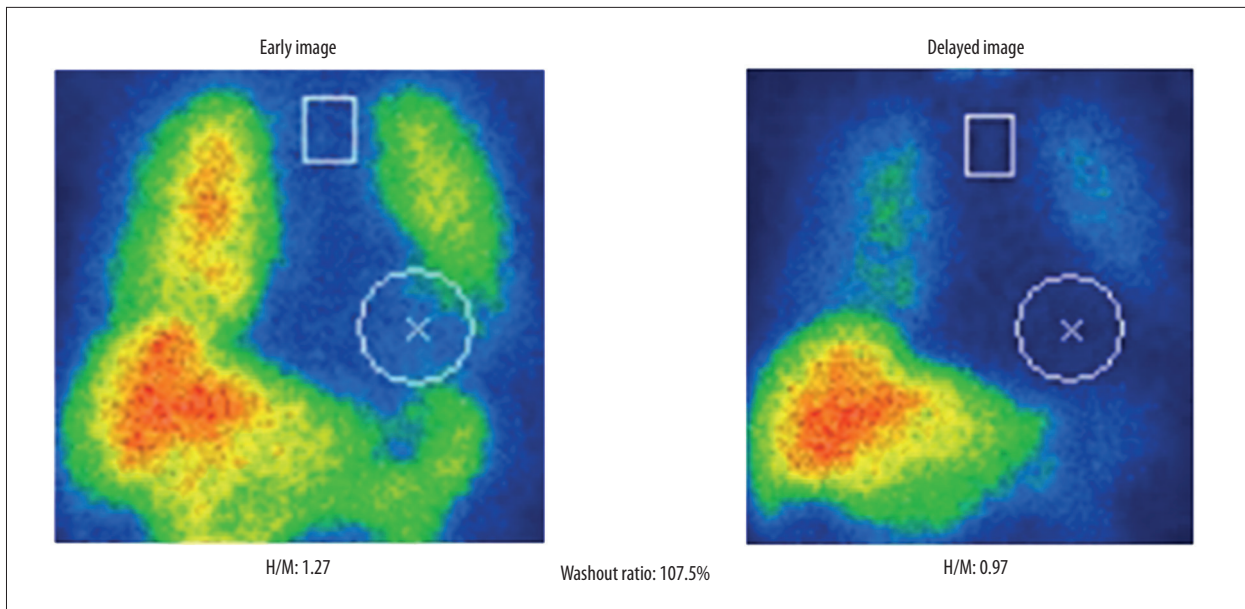


Figure 7. H/M ratio on MIBG scintigraphy after the administration of sitagliptin.

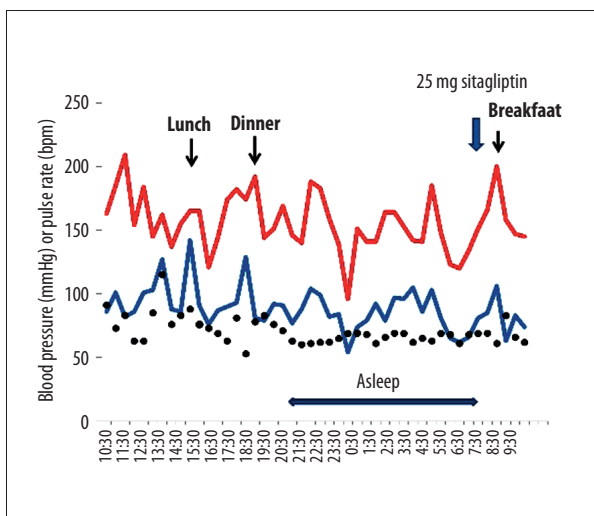


Figure 8. 24-hour ambulatory blood pressure monitoring, under the administration of sitagliptin, after one-year follow-up. Ambulatory blood pressure monitoring was performed at 30-minute intervals for 24 hours.

mechanism responsible for the postprandial hypotension. The administration of sitagliptin, a DPP-4 inhibitor, reduced the patient's postprandial hypotension, and moreover, it reduced orthostatic hypotension by increasing sympathetic nervous system activation. The amelioration of the patient's hypotensive episodes also resulted in an improvement in her cognitive function.

The mechanism responsible for postprandial hypotension is poorly understood. The intake of carbohydrates induces the secretion of insulin and neurotensin, which in turn increase mesenteric arterial flow and portal venous flow, leading to

peripheral vascular dilatation. Patients with autonomic nervous system dysfunction display delay compensatory blood pressure rises and are likely to suffer hypotensive episodes. Recently, Vanis et al. [3,4] reported that the administration of saline to the stomach did not induce postprandial hypotension, but the administration of glucose did. These findings showed that the postprandial hypotension induced by glucose was not caused by dilation of the gastroenterological system, which is considered to cause hypotension and dumping syndrome. Glucagon-like peptide-1 (GLP-1) secretion might affect the causative mechanism of postprandial hypotension, as GLP-1 was reported to enhance glucose-dependent insulin secretion and to delay gastric emptying.

In this present case report, the patient's orthostatic hypotension was reduced, but the mechanism responsible for this was unclear. The reactivity of the patient's sympathetic nervous system, which was measured as the change in the LF/HF ratio observed after standing up, was improved after the administration of sitagliptin. No previous studies have found that DPP-4 inhibitors attenuate autonomic function, and therefore, we need to clarify the mechanism responsible for this by further study of patients.

In patients with dementia with Lewy bodies, postprandial and orthostatic hypotension contributes to cognitive decline. However, these aspects of the condition might be treatable. It has been reported that excessively low blood pressure in medicated hypertensive patients was associated with cognitive impairment [5]. The administration of α -glucosidase inhibitors or DPP-4 inhibitors could be used to prevent excessive blood pressure reductions in patients with autonomic dysfunction.

Additionally, some experimental studies have demonstrated that GLP-1 agonists and DPP-4 inhibitors had direct neuro-
nal effects, leading to improvement of cognitive function [6].

Conclusions

We report on a case of postprandial hypotension and ortho-
static hypotension due to autonomic dysfunction in a patient

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with dementia with Lewy bodies. The administration of the DPP-4 inhibitor sitagliptin improved the patient's postprandial hypotensive episodes, as well as her episodes of orthostatic hypotension, by modifying the reactivity of her sympathetic nervous system. The patient did not suffer any adverse effects of sitagliptin treatment. The amelioration of the patient's hypotensive episodes led to an improvement in her cognitive function.