Effects of exenatide on metabolic parameters/control in obese Japanese patients with type 2 diabetes

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Abstract. The effects of exenatide on glycemic control, lipid metabolism, blood pressure, and gastrointestinal symptoms were investigated in obese Japanese patients with type 2 diabetes mellitus. Twenty-six outpatients were enrolled and administered 5 μg of exenatide twice daily. If there was insufficient weight loss and/or insufficient improvement in glycemic control, the dose was increased to 10 μg twice daily. Follow-up was continued until the 12th week of administration. Hemoglobin A1c, glycoalbumin, fasting plasma glucose, body weight, fasting serum C-peptide, serum lipids, blood pressure, and pulse rate were measured before and after the observation period. In the initial phase of exenatide therapy, each patient received a diary to record gastrointestinal symptoms. During treatment with exenatide, hemoglobin A1c decreased significantly and serum C-peptide increased significantly. Body weight, low-density lipoprotein cholesterol, and systolic blood pressure decreased significantly. Nausea was the most frequent gastrointestinal symptom and occurred in 16 patients. Its onset was noted at a mean of 1.7 h after injection, the mean duration was 1.1 h, and it continued for a mean of 9.3 days after the initiation of administration. Patients with nausea showed a significant decrease in hemoglobin A1c, glycoalbumin, or body weight compared with those without nausea. These findings suggest that a more marked improvement in metabolic parameters by exenatide can be partly dependent on the manifestation of gastrointestinal symptoms.

Key words: Type 2 diabetes mellitus, Obesity, Exenatide, Incretin

EXENATIDE is a human glucagon-like peptide-1 (GLP-1) receptor agonist produced by solid-phase peptide synthesis that has the same amino acid sequence as exendin-4, which was isolated from the saliva of the Gila monster (Heloderma suspectum). Similar to endogenous active GLP-1, exenatide specifically binds to GLP-1 receptors (seven-transmembrane, G protein-coupled receptors) and activates adenylate cyclase to increase the intracellular concentration of cyclic AMP in β-cells, leading to a decrease in plasma glucose levels by promoting glucose-dependent insulin secretion. In addition to the suppression of increased glucagon secretion, exenatide promotes weight loss caused by delayed gastric emptying and/or suppression of food intake through the satiety effect [1].

The most frequent gastrointestinal symptoms caused by exenatide are nausea, vomiting, diarrhea, and constipation, which may be related to delayed gastric emptying, suppressed food intake and enhanced colonic motility, although the detailed mechanisms have yet to be clarified.

Few reports have been published on the effects of exenatide on glycemic control and gastrointestinal symptoms in obese Japanese patients with type 2 diabetes. Therefore, we investigated the effects of exenatide on metabolic parameters such as plasma glucose, lipids, blood pressure, and body weight and evaluated the associated gastrointestinal symptoms in Japanese obese patients with type 2 diabetes.

Patients and Methods

Patients
From August 2011 to September 2012, 26 obese
outpatients with type 2 diabetes mellitus were enrolled in this study (obesity is defined by a body mass index (BMI) of ≥25 kg/m² in Japan). All patients had inadequate glycemic control after more than 6 months of treatment with oral hypoglycemic agents and insulin in addition to diet and exercise. Other enrollment criteria for this study were as follows: hemoglobin A1c (HbA1c; NGSP) ≥7.0%; BMI ≥25 kg/m²; and fasting serum C-peptide reactivity (CPR) ≥1.0 ng/mL.

Exclusion criteria included severe hepatic/renal disorders, severe infection, recent or scheduled surgery, severe trauma, and other factors deemed inappropriate by the attending physician.

Previous medications included insulin in 9 patients (38%), dipeptidyl peptidase 4 (DPP-4) inhibitor in 10 (42%), sulfonylureas in 11 (46%), metformin in 9 (38%), α-glucosidase inhibitor (α-GI) in 5 (21%), thiazolidinedione in 3 (13%), and diet and exercise alone in 3 (13%).

Study design

The effects of additional treatment with exenatide were assessed in week 12.

Various metabolic parameters such as body weight, fasting plasma glucose, HbA1c (NGSP), glycoalbumin (GA), serum CPR, lipids (low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides), and blood pressure (systolic and diastolic) were measured before treatment (week 0) and in week 12 of exenatide treatment.

For initial treatment, 5 μg of exenatide was subcutaneously administered twice a day (30 min before breakfast and 30 min before dinner). When weight reduction or improvement in HbA1c was not observed by week 4 in comparison with week 0, the dosage was increased to 10 μg twice daily until week 12. Oral hypoglycemic agents used prior to exenatide treatment were continued at the same dose; however, insulin, DPP-4 inhibitor and α-glucosidase inhibitor were discontinued. Other drugs were not added or changed during the study period. At the start of exenatide administration, a diary was given to each patient so that a daily record of the presence/absence and details of any gastrointestinal symptoms could be maintained.

Initial analysis was conducted for all patients, who were then divided into two groups: a group in which nausea was the most frequent gastrointestinal symptom during the period from the start of exenatide administration until week 12 and a group in which nausea was not reported throughout the study period. The relationship between each parameter and gastrointestinal symptoms was then assessed.

The aims of the study were explained to all patients and written informed consent was obtained. Moreover, this study was approved by the ethical committee of Hyogo College of Medicine and was conducted according to the Declaration of Helsinki.

Statistical analysis

StatView ver. 5.0 (SAS Institute Inc, Cary, NC, USA) was used for statistical analyses. The paired t-test or Wilcoxon signed-rank test was used for the comparison of parameters between Week 0 and Week 12, while the unpaired t-test or the Mann–Whitney test was used for comparison between the two groups. Statistical significance was set at $p < 0.05$. Simple correlations (Pearson) were used to assess the correlation of the number of days when nausea occurred, the total duration of nausea, and the time of occurrence after exenatide injection with the following parameters: HbA1c, GA, body weight, BMI, CPR, lipids (LDL cholesterol, HDL cholesterol, triglycerides), and blood pressure. Results are expressed as mean ± SD.

Results

Results for all patients (24 patients, excluding 2 dropouts)

The patient profiles are shown in Table 1. Of the 26 enrolled patients, 2 discontinued the study within 4 weeks of starting exenatide treatment because of severe gastrointestinal symptoms (nausea and vomiting). In the remaining 24 patients, HbA1c decreased significantly between week 0 and week 12 (9.3%–8.0%, $p = 0.004$) (Fig. 1a). GA also showed a significant change (23.4%–20.4%, $p = 0.033$) (Fig. 1b). No significant change was found in fasting plasma glucose (166–164 mg/dL;) (Fig. 1c). However, a significant increase in fasting CPR was observed (2.18–2.89 ng/mL; $p = 0.0028$) (Fig. 1d). Weight loss was significant (75.2–71.4 kg; $p < 0.0001$) (Fig. 2a), with a consequent decline in BMI (28.8–27.4 kg/m²; $p < 0.0001$) (Fig. 2b). Furthermore, a significant decrease in systolic blood pressure (136–130 mmHg; $p = 0.008$) (Fig. 2c) was observed, whereas diastolic blood pressure showed no significant change (79–78 mmHg;) (data not shown). There was a significant decrease in LDL cholesterol (121–110 mg/dL; $p = 0.023$) (Fig. 2d), whereas no significant change was observed in HDL cholesterol.
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who received 12 weeks of exenatide administration were divided into two groups. One group of 14 patients experienced nausea, and the other group of 10 did not experience nausea throughout the study period. Comparison of these two groups revealed that the group with nausea showed a significant decrease in HbAlc (9.0%–7.5%, \(p = 0.0167\)) (Fig. 1a) and GA (22.1%–18.0%; \(p = 0.0171\)) (Fig. 1b) between week 0 and week 12. There was no significant change in fasting plasma glucose (158–146 mg/dL) (Fig. 1c). In the group without nausea, there was no significant change in HbAlc (9.6%–8.7%) (Fig. 1a) or GA (25.2%–23.7%) (Fig. 1b). Fasting plasma glucose increased from 178 mg/dL to 190 mg/dL, but the change was not significant (\(p = 0.609\)) (Fig. 1c).

The group with nausea showed no significant change in fasting serum CPR from week 0 to week 12 (Fig. 1d), whereas the group without nausea showed a significant increase (2.22–3.48 ng/mL; \(p = 0.002\)) (Fig. 1d).

Body weight decreased significantly (72.2–68.1 kg; \(p = 0.0003\)) (Fig. 2a) in the group with nausea, with a consequent decline in BMI (28.7–26.9 kg/m\(^2\); \(p = 0.0003\)) (Fig. 2b). Significant weight loss was also observed in the group without nausea (79.3–76.2 kg; \(p = 0.012\)) (Fig. 2a), with a consequent decline in BMI (29.2–27.9 kg/m\(^2\); \(p = 0.015\)) (Fig. 2b). The decrease was greater in patients with nausea than in those without.

### Table 1 Patient profiles

<table>
<thead>
<tr>
<th></th>
<th>total (n = 24)</th>
<th>with nausea (n = 14)</th>
<th>without nausea (n = 10)</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male : female)</td>
<td>10 : 14</td>
<td>5 : 9</td>
<td>5 : 5</td>
<td>n.s</td>
</tr>
<tr>
<td>Age (y)</td>
<td>57.3±13.2</td>
<td>59.7±11.8</td>
<td>54.0±14.3</td>
<td>n.s</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.8±10.7</td>
<td>158.3±10.6</td>
<td>164.3±9.9</td>
<td>n.s</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>75.2±13.9</td>
<td>72.2±12.9</td>
<td>79.3±14.2</td>
<td>n.s</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>28.9±2.9</td>
<td>28.7±2.9</td>
<td>29.2±2.9</td>
<td>n.s</td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>9.5±7.9</td>
<td>8.3±7.6</td>
<td>11.9±8.0</td>
<td>n.s</td>
</tr>
<tr>
<td>HbA1c (NGSP) (%)</td>
<td>9.3±1.3</td>
<td>9.0±1.5</td>
<td>9.6±0.7</td>
<td>n.s</td>
</tr>
<tr>
<td>GA(%)</td>
<td>23.4±4.8</td>
<td>22.1±4.8</td>
<td>25.2±4.2</td>
<td>n.s</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dL)</td>
<td>166±47</td>
<td>158±34</td>
<td>178±60</td>
<td>n.s</td>
</tr>
<tr>
<td>Fasting plasma CPR (ng/mL)</td>
<td>2.2±1.2</td>
<td>2.2±1.0</td>
<td>2.2±1.5</td>
<td>n.s</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>136±16</td>
<td>141±17</td>
<td>129±12</td>
<td>n.s</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>79±14</td>
<td>81±13</td>
<td>77±15</td>
<td>n.s</td>
</tr>
<tr>
<td>Pulse rate (bpm)</td>
<td>82±10</td>
<td>83±9</td>
<td>81±12</td>
<td>n.s</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>121±27</td>
<td>121±26</td>
<td>124±40</td>
<td>n.s</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>51±13</td>
<td>50±10</td>
<td>53±17</td>
<td>n.s</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>163±76</td>
<td>176±70</td>
<td>146±81</td>
<td>n.s</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

n.s., not significant; GA, glycoalbumin; CPR, C-peptide reactivity; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-cholesterol, low-density lipoprotein cholesterol; HDL-cholesterol, high-density lipoprotein cholesterol

(51–49 mg/dL; data not shown) and triglycerides (163–167 mg/dL; data not shown).

**Gastrointestinal symptoms**

Among the confirmed gastrointestinal symptoms, nausea was the most common, occurring in 16 of the original 26 patients (62%) who received exenatide (Table 2). Vomiting occurred in 3 patients (12%) and diarrhea in 2 (8%).

In the patients who developed nausea, the mean time of onset after exenatide injection was 1.6 ± 1.2 h, while the mean duration of each episode was 1.1 ± 0.5 h. Nausea occurred for a mean of 9.3 ± 6.4 days from the initiation of administration.

There was no case in which gastrointestinal symptoms reappeared or newly appeared after the dose of exenatide was increased to 10 μg 4 weeks after the initiation of administration.

**Correlation of gastrointestinal symptoms with metabolic parameters**

Correlations of the number of days for which nausea occurred, the time of onset, and the duration of each episode with metabolic parameters such as HbA1c, GA, serum CPR, lipids, body weight, BMI, and blood pressure were investigated in all 24 patients. No significant correlations were observed. Then, the patients who received 12 weeks of exenatide administration were divided into two groups. One group of 14 patients experienced nausea, and the other group of 10 did not experience nausea throughout the study period. Comparison of these two groups revealed that the group with nausea showed a significant decrease in HbA1c (9.0%–7.5%, \(p = 0.0167\)) (Fig. 1a) and GA (22.1%–18.0%; \(p = 0.0171\)) (Fig. 1b) between week 0 and week 12. There was no significant change in fasting plasma glucose (158–146 mg/dL) (Fig. 1c). In the group without nausea, there was no significant change in HbA1c (9.6%–8.7%) (Fig. 1a) or GA (25.2%–23.7%) (Fig. 1b). Fasting plasma glucose increased from 178 mg/dL to 190 mg/dL, but the change was not significant (\(p = 0.609\)) (Fig. 1c).
Fig. 1 Changes in HbA1c (a), GA (b), FPG (c), and fasting plasma CPR (d) with exenatide

* $p < 0.05$; ** $p < 0.005$; n.s., not significant

GA, glycoalbumin; FPG, fasting plasma glucose; CPR, C-peptide reactivity
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Fig. 2 Changes in body weight (a), BMI (b), SBP (c), and LDL cholesterol (d) with exenatide

*p < 0.05; **p < 0.005; n.s., not significant

BMI, body mass index; SBP, systolic blood pressure; LDL-chol, low-density lipoprotein cholesterol
The group with nausea showed a significant decrease in systolic blood pressure between week 0 and week 12 (141–133 mmHg; \( p = 0.0208 \)) (Fig. 2c), but no significant change was observed in diastolic blood pressure and pulse rate (data not shown). The group without nausea showed no significant changes in systolic blood pressure, diastolic blood pressure, and pulse rate.

The group with nausea showed a significant decrease in LDL cholesterol (was observed) (125–105 mg/dL; \( p = 0.0133 \)) (Fig. 2d), but no significant change in HDL cholesterol and triglycerides (data not shown) between week 0 and 12. The group without nausea showed no significant change in LDL cholesterol (Fig. 2d), HDL cholesterol, and triglycerides (data not shown).

### Table 2  Gastrointestinal symptoms (n = 26)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>Nausea (%)</td>
<td>16 (62)</td>
</tr>
<tr>
<td>Vomiting (%)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>The time when nausea appears after injection (h)</td>
<td>1.6±1.2</td>
</tr>
<tr>
<td>The duration of nausea continued (h)</td>
<td>1.1±0.5</td>
</tr>
<tr>
<td>The days which nausea follows (day)</td>
<td>9.3±6.4</td>
</tr>
</tbody>
</table>

**Effects of prior treatment with insulin and DPP-4 inhibitor on plasma glucose, CPR and body weight**

HbA1c in 9 patients treated with insulin prior to the treatment with exenatide (insulin group) was 9.1 ± 1.2% at week 0 and 8.6 ± 1.9% at week 12, showing no statistically significant difference \( (p=0.4632) \). Fasting plasma glucose was 142 ± 45 and 180 ± 53 mg/dL, at week 0 and 12, respectively, also showing no statistically significant difference \( (p=0.1872) \). HbA1c in 15 patients not treated with insulin prior to the use of exenatide (non-insulin group) was 9.4 ± 1.3% and 7.7 ± 1.2% at week 0 and 12, respectively, showing a significant decrease \( (p=0.0036) \). Fasting plasma glucose was 181 ± 43 and 155 ± 45 mg/dL at week 0 and 12, respectively, showing a significant decrease \( (p=0.0413) \).

Fasting CPR in the insulin group increased significantly from 1.48 ± 1.3 ng/mL at week 0 to 3.01 ± 1.32 ng/mL at week 12 \( (p=0.0008) \), while the non-insulin group showed no significant change from 2.59 ± 1.0 ng/mL to 2.82 ± 0.76 ng/mL \( (p=0.3074) \).

Body weight in the insulin group showed a significant decrease from 70.6 ± 8.4 kg at week 0 to 66 ± 9.2 kg at week 12 \( (p=0.0048) \), with a consequent decrease in BMI \( (27.9 ± 2.2 to 26.3 ± 1.8, p=0.0057) \). The non-insulin group also showed a significant decrease in body weight from 77.9 ± 15.7 kg to 74.4 ± 16.4 kg \( (p=0.0009) \), with a consequent decrease in BMI \( (29.5 ± 3.1 to 28.0 ± 3.3, p=0.001). \)

In 10 patients treated with DPP-4 inhibitor prior to the use of exenatide (DPP-4 inhibitor group), HbA1c showed a downward tendency (9.6 ± 0.9% to 8.4 ± 1.6%, \( p=0.0817 \)) and fasting plasma glucose no significant change \( (185 ± 46 to 173 ± 54 mg/dL, p=0.5075) \).

In 14 patients not treated with DPP-4 inhibitor prior to the use of exenatide (non-DPP-4 inhibitor group), HbA1c was 9.0 ± 1.5% at week 0 and 7.6 ± 1.5% at week 12, showing a significant decrease \( (p=0.0324) \). Fasting plasma glucose in this group was not significantly changed \( (153 ± 44 to 158 ± 45 mg/dL, p=0.7977) \).

In the case of fasting CPR, no significant change was observed in the DPP-4 inhibitor group \( (2.79 ± 1.18 to 3.08 ± 1.47 ng/mL, p=0.3438) \), whereas a significant increase was observed in the non-DPP-4 inhibitor group \( (1.73 ± 1.1 to 2.75 ± 1.25 ng/mL, p=0.0031) \).

Body weight decreased significantly in the DPP-4 inhibitor group \( (78.0 ± 15.1 to 74.3 ± 16.1 kg, p=0.0096) \) with consequent decrease in BMI \( (29.2 ± 2.7 to 27.7 ± 3.1, p=0.0109) \). A significant decrease in body weight was also observed in the non-DPP-4 inhibitor group \( (73.1 ± 12.6 kg to 69.1 ± 13.1 kg, p=0.0004) \), with a consequent decrease in BMI \( (28.7 ± 3.0 to 27.1 ± 2.9, p=0.0005) \).

### Discussion

In this study, we investigated the effects of exenatide on glycemic control, body weight, lipids, blood pressure, pulse rate, and gastrointestinal symptoms in obese Japanese patients with type 2 diabetes.

Assessment of the 24 patients treated for 12 weeks revealed a significant decrease in HbA1c by 1.5%. Body weight decreased and fasting serum CPR increased significantly. These results suggest that exenatide therapy not only decreases HbA1c by enhancing endogenous insulin secretion but also achieves weight reduction. Because nausea was observed in 14 patients (58%), the influence of gastrointestinal symptoms on plasma glucose levels and metabolic parameters was assessed by dividing the patients into two groups with or without nausea. Although body weight decreased significantly in both groups, HbA1c and GA decreased significantly only in the patients with nausea (Fig. 1a, 1b). In the patients without nausea, serum CPR increased significantly (Fig. 1d), but there was no improvement in plasma glucose (Fig. 1c).

Because there was no significant change in fasting
plasma glucose despite a significant decrease in HbA1c and improvement in GA, suppression of postprandial hyperglycemia seemed to be greater with exenatide treatment, although this effect appeared to be weaker in the patients without nausea. Improvement in glycemic control by exenatide was more difficult to achieve in the patients without nausea, most probably because of the influence of changes in postprandial hyperglycemia. The occurrence of nausea during exenatide administration is thought to be related to its action on the digestive tract through the vagus nerve; this action was presumably stronger in the patients with nausea than in those without. Suppression of gastrointestinal, particularly gastric, motility seems to control postprandial hyperglycemia. In addition, delayed gastric emptying may have led to decreased food intake and appetite suppression, resulting in better control of postprandial blood glucose levels.

In contrast, suppression of appetite was not observed in most patients without nausea. Accordingly, the reason for the weaker effect of exenatide on HbA1c and GA in the patients without nausea was thought to be weaker inhibition of gastrointestinal motility, leading to less improvement in postprandial hyperglycemia.

In both healthy subjects and patients with diabetes who receive exogenous GLP-1, delay of gastric emptying after liquid and solid meal intake has been reported [2, 3]. This effect is GLP-1-dependent and is also observed physiologically after food intake. The regulation of gastric emptying has a great influence on the postprandial blood glucose response, so whether gastric emptying is delayed by exenatide or not may have a marked difference of effect on postprandial blood glucose.

The timing of the onset of nausea, its duration, and the time of occurrence after the initiation of exenatide administration differed greatly among the patients, and these variations were assumed to affect postprandial blood glucose. When exenatide is initiated, attention should be paid to nausea, particularly for about 3 h after dosing and for about 10 days from the start of administration.

Assessment of all patients showed a significant increase in serum CPR, with an improvement in glycemic control (Fig. 1a, b, d). In contrast, improvement in glycemic control was not observed in the patients without nausea, although there was an increase in fasting serum CPR (Fig. 1d).

We assessed the effect of the treatment with insulin and DPP-4 inhibitor prior to the treatment with exenatide on plasma glucose and body weight. In the case of DPP-4 inhibitor, patients with and without the prior treatment showed similar decreases in fasting plasma glucose and body weight. In the case of insulin, similar improvement in body weight was observed in patients with and without the prior treatment. However, patients with the prior insulin treatment failed to show improvement in HbA1c with worsened values of fasting plasma glucose in spite of an increase in fasting CPR.

Three of 15 patients with nausea and 6 of 9 patients without nausea were found to belong to a group of patients who received prior treatment with insulin. The fact that a large number of nausea-free patients were found in the insulin group is likely related to an increase in fasting plasma glucose and no improvement in HbA1c in spite of an increase in fasting CPR. Improvement in HbA1c was observed in patients with nausea who showed no significant increase in fasting CPR, suggesting that improvement in glycemic control/plasma glucose levels by exenatide is due not only to promotion of endogenous insulin secretion but also to aforementioned delay in gastric emptying or suppression of glucagon secretion (not investigated in this study).

Exenatide administration also resulted in a significant decrease in systolic blood pressure and LDL cholesterol with improvement in blood pressure and lipid metabolism (Fig. 2c, 2d).

It has already been reported that exenatide improves lipid metabolism in patients with type 2 diabetes and patients with impaired glucose tolerance.

Control of sodium reabsorption in the proximal renal tubules [4], suppression of phosphorylation of extracellular signal-regulated kinase by angiotensin II in the kidneys [5], and improvement in vasodilation by increasing NO (nitric oxide) production in vascular endothelial cells [6] are considered to be the mechanisms underlying the antihypertensive action of exenatide.

A previous study into the effect of GLP-1 agonist therapy on lipid metabolism in patients with type 2 diabetes or impaired glucose tolerance also showed that exenatide improves lipid metabolism [7].

Improvement in systolic blood pressure and LDL cholesterol was more marked in the patients with nausea. The total food intake and sodium intake were not controlled during the 12-week administration period of this study, which is considered to be one potential reason for the significant improvement in lipids and blood.
blood pressure only in the patients with nausea. It has been reported that LDL cholesterol is improved by long-term administration of exenatide [8]; therefore, a longer observation period is necessary in future studies.

It has been reported that obese people are often associated with characteristic eating behavior, such as overeating, lack of a sense of fullness, desire for fatty/lipid-rich foods and short mealtime [9]. In the present study, medical interviews revealed that patients treated with exenatide ate less snacks and fatty/lipid-rich foods and took a longer time for eating. These results suggest that changes in the amount of food, eating manner and favorite food play a role in improving body weight and blood pressure.

The body weight control could be a key factor for reduction of risks of cardiovascular events and diabetes complications. The present study indicates that exenatide decreases body weight and effectively improves both HbA1c and body weight particularly in patients with gastrointestinal symptoms.

Disclosure

None of the authors have any potential conflicts of interest associated with this research.

References