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Case Report

Effectiveness of sitagliptin in a patient with late dumping syndrome after total gastrectomy

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ABSTRACT

An 83-year-old man developed hypoglycemia after undergoing total gastrectomy for gastric cancer in 200X-4. The patient was admitted to our hospital in May 200X and placed on continuous glucose monitoring (CGM). Glycemic excursions were examined while on 3-meal/day (1700 kcal) and 6-meal/day (1800 kcal) diets. Oxyhyperglycemia followed about 2 h later by a sudden drop in glucose levels was seen with both regimens. These findings were consistent with late dumping syndrome. CGM was continued, oral miglitol at 150 mg/day or sitagliptin at 50 mg/day was started, and glycemic excursions were compared. Results were similar for both drugs, with reductions in postprandial glucose elevations. Meal tolerance testing 3 months after oral sitagliptin, compared to before starting treatment, showed reductions in both early postprandial hyperglycemia and insulin hypersecretion. These findings suggest that DPP-4 inhibitors such as sitagliptin may be effective for treating post-gastrectomy late dumping syndrome.

1. Introduction

Late dumping syndrome, characterized by a rapid influx of carbohydrates into the upper jejunum, rapidly increases absorption into the intestine, insulin hypersecretion due to oxyhyperglycemia, and clinical hypoglycemia 2 to 3 h after eating. The usefulness of treating late dumping syndrome with α-glucosidase inhibitors is increasingly being reported, [1–3]. but problems include treatment adherence and adverse reactions such as ileus. GLP-1 analogs have also recently been reported as useful for late dumping syndrome in patients after gastric bypass surgery [4]. With GLP-1 analogs as treatment in patients with type 2 diabetes, similar degrees of glucose lowering by the inhibition of glucagon secretion and promotion of insulin secretion have been reported [5]. The DPP-4 inhibitor sitagliptin is also reported to improve glucose-responsive insulin secretion and improve glucose levels without changing the amount of insulin secretion [6]. We believed that the multiple mechanisms of action of DPP-4 inhibitor other than promotion of insulin secretion, such as suppression of glucagon secretion, would improve glycemia without causing insulin hypersecretion. We administered sitagliptin to a post-gastrectomy patient with late dumping syndrome. At 90 days after starting sitagliptin, we evaluated the effects on improving early insulin secretion, postprandial hyperglycemia, and insulin hypersecretion. We believe that DPP-4 inhibitors such as sitagliptin may be useful for treating late dumping syndrome in post-gastrectomy patients.

2. Case report

Patient: An 83-year-old man.

Chief complaint: Hypoglycemic attacks.

Coexisting diseases: Hypertension and hyperlipidemia (no history of abnormal glucose tolerance).

Past medical history: Open total gastrectomy (Roux-en-Y procedure) for stage 3A gastric cancer (at 79 years old), acute cholecystitis (at 82 years old), and acute anterior wall myocardial infarction (at 83 years old).

Family history: Nothing of note.

Lifestyle history: Retired and lives with wife. Smoking: 20 cigarettes/day ×35 years. Alcohol: 180 ml of sake/day. Diet: Enjoys carbohydrates. Since being advised to eat smaller split meals by another clinic, now eats 5 times/day (standard 3 meals plus snacks such as rolled sushi, sponge cake, and orange juice at 10:00 and 15:00). Exercise: Walks 2.5 to 3 km every day.

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Medications: Aspirin 100 mg/day, clopidogrel sulfate 75 mg/day, rosuvastatin 2.5 mg/day, carvedilol 10 mg/day, magnesium oxide 1320 mg/day, and mecobalamin 1500 μg/day.

2.1. History of present illness

The patient underwent open total gastrectomy for gastric cancer at 79 years old in 200X-4. Postoperatively, he began experiencing hypoglycemic attacks approximately 2 to 3 times per year. Although the frequency of hypoglycemic attacks increased since 200X (at 83 years old), hypoglycemic symptoms were sometimes masked because of oral carvedilol. He always carried a snack with him to prevent hypoglycemia.

In March 200X (at 83 years old), the patient developed impaired consciousness and was transported by ambulance to another hospital. He was hypoglycemic with a random blood glucose of 38 mg/dl, and so was admitted for further evaluation and treatment. Testing during that hospitalization showed high 30-min postprandial glucose and immunoreactive insulin (IRI) levels and hypoglycemic 2 to 3 h after eating. Late dumping syndrome was diagnosed. Smaller split meals were recommended, and the patient was discharged. However, he frequently lost consciousness and required ambulance transport after discharge from that hospital, so his personal physician referred him to our department. He was admitted to our department for further evaluation in May 200X.

2.2. Findings on hospital admission

Height 161.9 cm; weight 46.3 kg (maximum weight 58 kg at 70 years old); body mass index (BMI) 17.7 kg/m^2; axillary temperature 36.7 °C; blood pressure 99/48 mmHg; and heart rate 60 beats/min and regular. No conjunctival pallor was evident, heart sounds were normal without any murmurs, and lungs were clear on auscultation. The abdomen was flat, soft, non-tender, and with normal bowel sounds (no decrease or increase). A midline surgical scar was evident. No edema of the lower extremities was present.

2.3. Laboratory results on admission (Table 1)

BUN, 17.0 mg/dl; creatinine, 0.99 mg/dl; estimated glomerular filtration rate (eGFR) 55 ml/min/1.73 m^2; HbA1c 5.5%; glucose 71 mg/dl; IRI 5.3 μU/ml; and Homeostasis model assessment of β-cell function (HOMA-β) 238.5 (increased insulin secretion) Table 1.

Table 1
Laboratory data on admission. Homeostasis model assessment of β-cell function (HOMA-β) was 238.5 (increased insulin secretion).

[CBC]			[Endocrine]		
WBC	3.60	$\times10^3$/mm^3	FT4	1.0	ng/dl
RBC	3.85	$\times10^6$/mm^3	TSH	3.070	μIU/ml
HGB	12.1	g/dl	GH	0.40	ng/ml
HCT	36.1	%	IGF-1	73	ng/ml
PLT	15.1	$\times10^4$/mm^3	PRL	12.6	ng/ml
[Biochemistry]			LH	6.3	mIU/ml
AST	24	U/l	FSH	11.9	mIU/ml
ALT	15	U/l	F-teststerone	4.0	pg/ml
ALP	166	U/l	ACTH	51.2	pg/ml
LDH	230	U/l	Cortisol	14.3	μg/dl
LAP	49	U/l	Renin	0.1	ng/ml/h
γ-GTP	16	U/l	Aldosterone	60.0	pg/ml
Amy	132	U/l	[Spot urine]		
CK	61	U/l	Specific gravity	1.012	
TP	6.0	g/dl	pH	7.0	
Alb	3.4	g/dl	Protein	(−)	
T-Bil	0.3	mg/dl	Glucose	(−)	
BUN	17.0	mg/dl	Blood	(−)	
Cre	0.99	mg/dl	Ketone	(−)	
eGFR	55	ml/min/1.73 m^2	[24 h urine]		
UA	5.8	mg/dl	Protein	96	mg/day
Na	141	mEq/l	Glucose	0.019	g/day
K	4.3	mEq/l	Cre	0.864	g/day
Cl	106	mEq/l	Alb	11.5	mg/day
Ca	8.2	mg/dl	CPR	113.9	μg/day
LDL-Cho	40	mg/dl			
HDL-Cho	58	mg/dl			
TG	42	mg/dl			
BG	71	mg/dl			
HbA1c(NGSP)	5.5	%			
CRP	0.03	mg/dl			
IRI	5.3	μU/ml			
1,5-AG	15.6	μg/ml			
GA	14.9	%			
CPR	3.17	ng/ml			

2.4. Post-admission clinical course

The clinical course up to this time had established a diagnosis of post-gastrectomy late dumping syndrome. Hypoglycemic symptoms became less noticeable with the initiation of oral carvedilol, so oral carvedilol was therefore temporarily discontinued after hospital admission. Anterior pituitary function was also monitored to evaluate other causes of hypoglycemia, but none were found.

Continuous glucose monitoring (CGM) was started after admission, and glycemic excursions were evaluated during a 3-meal/day (1700 kcal) diet and a 6-meal/day (1800 kcal) diet (Fig. 1). Although no severe hypoglycemic attack occurred, oxyhyperglycemia followed about 2 h later by a sudden drop in glucose level occurred with both diets. These findings were consistent with a diagnosis of late dumping syndrome. A carbohydrate-restricted diet (45% carbohydrates) was then started, and glycemic excursions were again evaluated by CGM during a 3-meal/day (1800 kcal) diet while taking oral miglitol at 150 mg/day, and oral sitagliptin at 50 mg/day (Fig. 2). Miglitol could hold hypoglycemia and hyperglycemia in comparison with sitagliptin. However, hypoglycemia and hyperglycemia are improved by the sitagliptin dosage in comparison with 6 split meals and a carbohydrate-ristricted diet.

After considering the fact that maintaining a carbohydrate-restricted diet after hospital discharge would be difficult, development of abdominal bloating with miglitol, potential problems with treatment adherence, and the habit of the patient to eat many in-between meal snacks, oral sitagliptin was selected as the most appropriate treatment for this patient. Oral sitagliptin was therefore continued and the patient was discharged.

During a clinic visit 90 days after hospital discharge while the patient was taking oral sitagliptin, a meal tolerance test was performed. Results were compared with a meal tolerance test performed before oral sitagliptin had been started (Fig. 3). Although no severe hypoglycemic attack occurred during meal tolerance test before oral sitagliptin, oxyhyperglycemia followed about 3 h later by a sudden drop in glucose level occurred. Treatment with oral sitagliptin suppressed not only the early secretion of insulin but also the early postprandial hyperglycemia and that resulted in improving insulin hypersecretion and the later hypoglycemia.

Oral sitagliptin was continued, and currently, about 2 year since hospital admission, there have been no more hypoglycemic attacks associated with loss of consciousness.

3. Discussion

Dietary therapy is the mainstay of treatment for late dumping syndrome, and carbohydrate and fluid restriction, smaller split meals, and avoidance of hyperosmolar meals can improve dumping symptoms. Alpha-glucosidase inhibitors, a class of

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