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Reactive hypoglycaemia due to late dumping syndrome: successful treatment with acarbose

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Summary

Reactive hypoglycaemia is a rare disease which occurs postprandially in everyday life involving blood glucose levels below 2.5 to 2.8 mmol/l. We report on a 66-year-old patient who developed symptomatic reactive hypoglycaemia due to late dumping syndrome 10 years after oesophagectomy with cervical anastomosis. A 75 g sucrose load revealed a plasma glucose level of 9.4 mmol/l after one hour, followed by symptomatic hypoglycaemia with a plasma glucose level of 1.8 mmol/l after three hours. Concomitantly, high concentrations of insulin (3216 pmol/l at a glucose level of 9.4 mmol/l and 335 pmol/l at a glucose level of 1.8 mmol/l) and glucagon-like peptide 1 (GLP-1) (375 pmol/l at a glucose level of 9.4 mmol/l and 85 pmol/l at a glucose level of 1.8 mmol/l) were measured. While the patient was under treatment with acarbose, another sucrose load did not provoke symptomatic hypoglycaemia (plasma glucose nadir of 4.6 mmol /l after two hours). Insulin and GLP-1 levels increased much less, to peak levels of 375 pmol/l and 75 pmol/l respectively, after one hour when plasma glucose was 6.8 mmol/l.

We conclude that in patients with reactive hypoglycaemia due to gastrointestinal surgery, acarbose decreases rapid glucose absorption associated with hyperglycaemia and GLP-1 secretion, and thus diminishes excessive insulin release. Acarbose is therefore a successful treatment modality for reactive hypoglycaemia due to late dumping syndrome.

Keywords: α-glucosidase inhibitor; reactive hypoglycaemia; dumping syndrome; treatment

Introduction

Reactive hypoglycaemia is a rare disease, defined as a clinical disorder in which hypoglycaemic symptoms occur postprandially in everyday life with a blood glucose level below 2.5 to 2.8 mmol/l. Reactive hypoglycaemia can be caused by fructose intolerance, galactosaemia, drugs, and by late dumping syndrome in patients who have undergone gastric or oesophageal surgery [1, 2]. Late dumping symptoms (sweating, fatigue, disturbed consciousness, tremor, tachycardia) result from a rapid rise and subsequent fall in blood glucose levels and appear 1–3 h after meals [3]. Most patients with dumping syndrome can be treated by advice on diet and lifestyle. In addition, several other treatments, including surgery or somatostatin, have been attempted to relieve late dumping symptoms [4, 5].

Administration of an α-glucosidase inhibitor offers protection against a postprandial increase in plasma glucose levels by inhibiting carbohydrate digestion, a measure generally adopted for treatment of diabetes mellitus type 2. Acarbose was found to flatten the glycaemic response to an oral sucrose load, preventing the late blood glucose fall in healthy individuals and in patients with symptomatic reactive hypoglycaemia [6–8]. We studied the effect of treatment with acarbose in a patient with severe reactive hypoglycaemia due to late dumping syndrome.

Case report

A 66-year-old male was admitted to our hospital with a 3-month history of increasing weakness, nausea, sweating, dizziness, and qualitative impairment of consciousness, usually occurring in the late morning. These symptoms disappeared immediately after carbohydrate ingestion. Ten years ago he underwent total thoracoabdominal oesophagectomy with cervical anastomosis for squamous cell carcinoma in the middle third of the oesophagus (pT2 N0 M0). Complete remission had been observed up to the present. Three months before admission the patient had changed his diet to high caloric soft drinks and chocolate because of increased dysphagia. On admission his general physical condition was good without signs of oesophageal cancer metastases. Neurological examination was normal. Full blood count, erythrocyte sedimentation rate and biochemical results including sodium, potassium, creatinine, liver enzymes, albumin, and TSH were normal. During the episodes of weakness, sweating, and dizziness venous plasma glucose levels were usually below 2.5 mmol/l. A prolonged fast over 72 hours revealed no hypoglycaemia. An oral 75 g glucose tolerance test showed symptomatic hypoglycaemia with a plasma glucose nadir of 0.8 mmol/l after 3 hours (Table 1). A load with 75 g sucrose, a substrate for α-glucosidase in the gut which is inhibited by acarbose, revealed a plasma glucose level of 9.4 mmol/l after one hour followed by symptomatic hypoglycaemia with a plasma glucose level of 1.8 mmol/l after three hours (Fig. 1). At the same time, high insulin- and glucagon-like peptide 1 (GLP-1) concentrations were measured. The two hormones, normal at baseline in our patient, rose excessively following the sucrose load (Fig. 2). These laboratory findings, in conjunction with the typical clinical presentation, provide evidence of reactive hypoglycaemia due to late dumping syndrome. In another sucrose load combined with 100 mg acarbose, an α-glucosidase inhibitor, symptomatic hypoglycaemia (plasma glucose nadir of 4.6 mmol /l) did not occur. This time the insulin concentration was more than 10 times lower, and the GLP-1 level 5 times lower compared to the levels during the sucrose load without acarbose (Fig. 2). In our patient the treatment with acarbose with the main meals consistently prevented further symptomatic hypoglycaemia.

Table 1

Oral glucose tolerance test (75 g).

	0 h	1 h	2 h	3 h	4 h
Plasma glucose (mmol/l)	4.8	9.7	5.6	0.8	2.7
Plasma C-peptide (pmol/l)	495	12 600	6300	300	960
Plasma insulin (pmol/l)	97	5829	1970	375	111

Figure 1

Plasma glucose (without ♦ / with acarbose ■) in 75 g sucrose load.

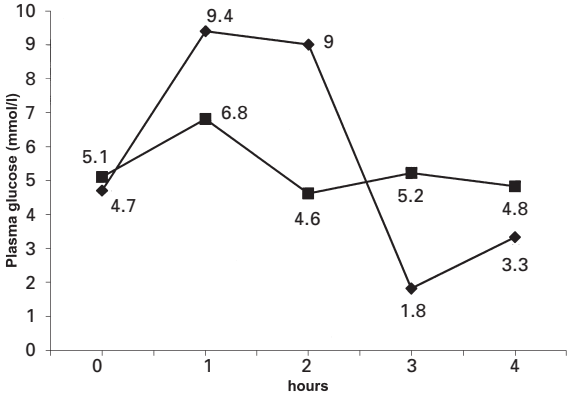
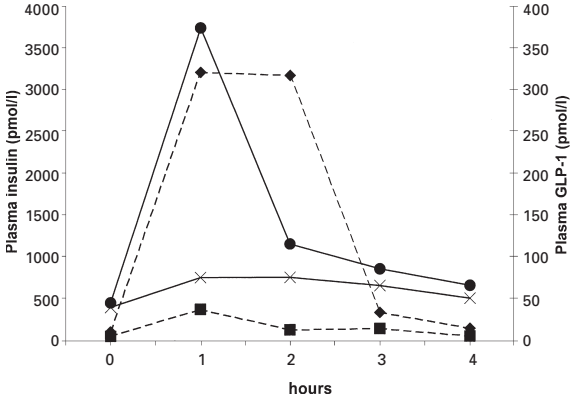


Figure 2

Plasma insulin (without – –♦– – / with acarbose – – ■ – –) and GLP-1 (without ● / with acarbose X) response to 75 g sucrose.



Discussion

The diagnosis of reactive hypoglycaemia due to late dumping syndrome was accurate in our patient because the following criteria were met: our patient had a history of total oesophagectomy ten years previously. Symptoms appeared 1–3 hours after the ingestion of meals, were coincident with low plasma glucose, were reproduced during the glucose tolerance test or sucrose loads (Table 1, Fig. 1), and were absent when the patient was normoglycaemic [9]. Moderate to severe dumping has

been reported in 8.5–20% after vagotomy and pyloroplasty, in 4–27% after vagotomy and antrectomy, in 10–40% after gastrectomy [3], and in over 50% after oesophagectomy [10]. The late dumping syndrome occurs 1–3 h after meals, when the fast delivery of food to the small intestine causes rapid glucose absorption and induces not only hyperglycaemia but also exaggerated secretion of the insulinotropic gut hormone GLP-1, which is chiefly produced by intestinal L-cells in the lower gastrointestinal tract. Hyperglycaemia and increased GLP-1 secretion account for excessive insulin release which, in turn, causes reactive hypoglycaemia (Fig. 2) [11]. On the other hand, it is impossible to induce hypoglycaemia with GLP-1 in subjects with normoglycaemia because its insulinotropic action is glucose-dependent and is weak or absent at normal basal state glucose concentrations [11]. There is another gut hormone which can function as an incretin, i.e. to further enhance insulin secretion: gastric inhibitory peptide (GIP). However, patients with late dumping syndrome following gastric surgery do not have increased GIP levels [12].

The most important measure in the treatment of late dumping syndrome is to avoid meals rapidly delivering large amounts of glucose for absorption by the small intestine. This can be done by dividing the food intake into at least five meals per day. Meals rich in carbohydrates can induce dumping syndrome, and therefore carbohydrates should be reduced. Another way of slowing rapid glucose absorption is treatment with acarbose, an α-glucosidase inhibitor. When our patient was treated with acarbose, reactive hypoglycaemia no longer occurred. Acarbose reversibly blocks α-glucosidase, which is responsible for breaking down complex carbohydrates in the intestine into absorbable monosaccharides. This causes delayed glucose absorption and a diminished rise in blood glucose after meals, resulting in a reduction of postprandial hyperglycaemia and insulin release [13], as shown in our patient. Reduced GLP-1 secretion also contributed to less excessive insulin release. An acarbose effect of this nature may be particularly beneficial for the patient with late dumping syndrome, and, to our knowledge, has not been reported before (Fig. 2). It should be noted that in hyperglycaemic type 2 diabetic patients, ingestion of acarbose with a sucrose load leads to elevated and prolonged GLP-1 release [14].

Thus, in patients with reactive hypoglycaemia due to gastrointestinal surgery, acarbose lowers the enteric stimuli for excessive insulin release and is therefore a successful treatment modality in avoiding reactive hypoglycaemia with its associated symptoms.

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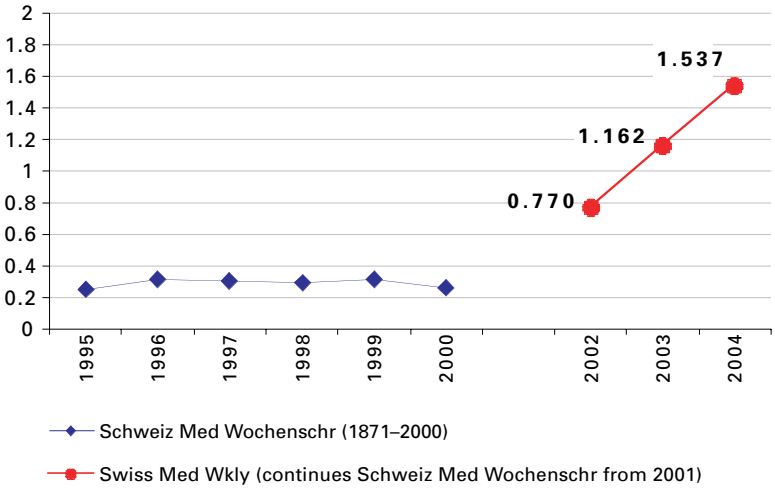

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