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Original article

Evaluation of carbohydrate restriction as primary treatment for post-gastric bypass hypoglycemia

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Abstract

Background: Up to 15% of patients who have undergone Roux-en-Y gastric bypass (RYGB) surgery may eventually develop symptoms of hypoglycemia.
Objectives: To evaluate the daily life efficacy of a carbohydrate (carb)-restricted dietary advice (CRD) of 6 meals per day with a 30 g carb maximum per meal in patients with documented post-RYGB hypoglycemia.
Setting: Teaching hospital, the Netherlands.
Methods: Frequency and severity of hypoglycemic events before and after CRD were assessed retrospectively in 41 patients with documented post-RYGB hypoglycemia, based on medical records and telephone questionnaires. Hypoglycemia was defined as a blood glucose level <3.0 mmol/L. Results are expressed as mean values ± standard error or median and range.
Results: CRD decreased the number of hypoglycemic events per month from 17.1 (1.5–180) to 2.5 (0–180), i.e., a decline of 85% ($P < .001$). The lowest blood glucose measured during a hypoglycemic event increased from 2.1 ± .4 to 2.6 ± .2 mmol/L ($P = .004$). The number of patients who had required outside help in the treatment of hypoglycemia, decreased from 23 to 6 ($P < .001$). In 14 patients (34.1%) the diet-induced reduction of hypoglycemia was insufficient and required the start of insulin suppressive therapy.
Conclusion: A CRD, consisting of 6 meals per day with up to 30 g carbs each, is an effective treatment of post-RYGB hypoglycemia in the majority of patients. Additional medication is needed in about a third of patients. (Surg Obes Relat Dis 2016;▮:00–00.)

Keywords: Roux-en-Y gastric bypass; Hypoglycemia; Carbohydrate restriction; Daily life efficacy

Bariatric surgery is a very successful treatment for morbid obesity, with sustained weight loss in the large majority of patients [1]. Roux-en-Y gastric bypass (RYGB) surgery is the most commonly performed procedure, accounting for about 45% of all bariatric procedures [2]. Despite its well-established clinical benefits, RYGB may also have adverse effects. Post-RYGB hypoglycemia, also known as "late dumping," is one of the late complications that has been recognized increasingly in recent years [3]. Symptoms include attacks of dizziness, perspiration, confusion, and even collapse [4]. The prevalence of post-RYGB hypoglycemia is not exactly known. Initial research, based on hospitalization rates, led to an estimated prevalence of .1%–.2% [5]. However, an analysis based on the

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presence of Whipple's triad, i.e., clinical signs of hypoglycemia in combination with a blood glucose level <3.0 mmol/L and resolution of the symptoms after glucose administration, found an incidence of 18% in a cohort of 351 patients [6,7]. In a questionnaire-based study, 34% of patients (n = 450) reported symptoms of hypoglycemia [8].

The most commonly proposed mechanism of post-RYGB hypoglycemia is hyperinsulinism, caused by pancreatic ß-cell hypertrophy and/or hyperplasia (nesidioblastosis) or by excessive glucagon-like peptide 1 (GLP-1) mediated ß-cell stimulation. Although nesidioblastosis has been shown to play a role in some cases it is generally considered to be very rare [9,10]. Nesidioblastosis is characterized by autonomic hypersecretion of insulin and should be considered in patients with fasting hyperinsulinemia [7]. Usually, however, patients present with symptoms of postprandial hypoglycemia. This has been attributed to food activated GLP-1 release, stimulating insulin secretion by its binding to specific ß-cell receptors [11]. It has been established that postprandial hypoglycemia in patients after RYGB can be prevented by administration of a GLP-1 receptor antagonist [12]. Other medical options are the use of Acarbose, Octreotide or Diazoxide. Reversal of RYGB and partial pancreas resection have been suggested as last resort options; with these procedures, hypoglycemia disappeared in 13/17 (76%) and 34/51 (67%) of cases, respectively [13].

Carbohydrate (carb) restriction appears to be a logical first step in the treatment of postprandial hypoglycemia after RYGB because it is likely to reduce postprandial insulin release [7]. The efficacy of extreme carb-restricted meals (0 and 2 g per meal) has been successfully demonstrated in clinical settings [14,15]. However, in daily life such diets are hardly feasible. Botros et al. evaluated the effects of a more moderate 30 g carb-restricted meal [16]. During a 6-hour in-hospital observation period under resting conditions, none of the patients developed hypoglycemic symptoms or glucose levels <3.0 mmol/L. Based on these findings, we developed a carb-restricted dietary advice (CRD) consisting of 6 meals per day with a 30 g carb maximum per meal. In the present study, the daily life efficacy of this CRD has been evaluated as a first-line treatment for patients with documented post-RYGB hypoglycemia.

Methods

This is a single center, retrospective, per protocol analysis of the efficacy of a CRD for the treatment of patients presenting with symptoms of hypoglycemia after RYGB. Our hospital is a referral center for bariatric surgery where 4 surgeons perform about 1200 bariatric procedures per year. Postoperatively, all patients are advised to eat small, frequent meals throughout the day and to eat slowly and thoroughly. The study was performed according to the regulations of the local ethical committee.

Patients

Eighty patients with symptoms suggestive of post-RYGB hypoglycemia (i.e., postprandial attacks of lightheadedness, perspiration, trembling, confusion, and even collapse, disappearing after ingestion of carbohydrates) were referred to the dietician for CRD, either by a surgeon or an internist. For inclusion in this study, additional criteria were set: 1) symptoms of hypoglycemia developed after RYGB in the absence of antidiabetic medication; 2) documented home glucose levels <3.0 mmol/L during an event with symptoms suggestive of hypoglycemia; 3) postoperative remission of diabetes mellitus (fasting glucose <6.0 mmol/L, and HbA1C <42 mmol/mol) with all previous antidiabetic medication discontinued for at least 6 months; 4) baseline screening performed by an endocrinologist; 5) understanding of the Dutch language; and 6) implementation of CRD for a period of at least 1 month without concomitant use of Acarbose, insulin suppressive medication, GLP-1 antagonists, or any other medication known to have an effect on blood glucose levels.

Methods

Patients reporting hypoglycemic symptoms were usually referred to the internist for evaluation and treatment. This consultation included recording of gender, age, medical history, medication, body mass index (BMI), lowest measured home glucose level, frequency at which hypoglycemic symptoms occurred, and the number of times outside help was required for treatment. A fasting blood sample was obtained as part of standard procedures for measurement of plasma glucose, HbA1C, insulin, C-peptide, glucagon, and cortisol levels.

Patients with documented blood glucose levels <3.0 mmol/L received oral instructions for CRD by the dietician, in person or by telephone and additionally in print or by email. Patients were instructed to use a diet consisting of 6 small meals per day with a 30 g carb maximum per meal.

Continuous glucose monitoring for 5 consecutive days (CGM, Freestyle Navigator II, Abbott, Hoofddorp, the Netherlands) was used to evaluate the efficacy of CRD in a subset of patients, usually those who still reported hypoglycemic events after CRD. The results of CGM were reviewed by the dietician and endocrinologist, and discussed with the patients. If diet-induced reduction of hypoglycemia was insufficient, medical treatment was added, either Diazoxide or Octreotide or a combination of both.

Data collection

Medical records were examined to collect the data about frequency and severity of hypoglycemia before CRD. The actual situation after CRD was assessed by telephone questionnaire. Frequency of hypoglycemia was recorded