Post Gastric Bypass Hypoglycemia: Four Cases Treated Successfully with Alphaglucosidase Inhibitor Therapy

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Post Gastric Bypass Hypoglycemia: Four Cases Treated Successfully with Alphaglucosidase Inhibitor Therapy

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Introduction

- Roux-en-y gastric bypass (GB) surgery has been increasingly employed to treat the morbidities of obesity
- In 2005, Service et al (1) reported hyperinsulinemic hypoglycemia in 6 GB patients who were found to have anatomic changes in islet cells
- Since that time, postprandial hypoglycemia has become increasingly recognized as a late complication of GB
- Carbohydrate (CHO) restriction is recommended as initial therapy but is not always effective in reducing hypoglycemia
- Alphaglucosidase inhibitor (AGI) therapy has been suggested as a second line therapy
- We report the first collection of GB hypoglycemic patients who were successfully treated with long-term AGI therapy

Case 1

- 42 F who underwent GB 3 years prior presented for evaluation of hypoglycemia
- Patient met criteria for Whipple's Triad:
  - Experienced sweating, palpitations, tremor and neuroglycopenic symptoms 2-4 hours postprandial
  - Documented capillary glucose (BG) of 35-50 mg/dl
  - Symptoms resolved with simple CHO
- Baseline testing ruled out adrenal, thyroid, renal and hepatic dysfunction
- Mixed 75g meal endocrine testing revealed:
  - Fasting BG 83 mg/dL
  - 115 minute symptomatic BG of 42 mg/dL with simultaneous serum insulin 14 ulU/mL (<29.2 ulU/mL)
  - C-peptide 4.2 ng/ml (0.9-6 ng/mL)
  - Beta hydroxybutyric acid of 0.08 mmol/L (0.0-0.42 mmol/L)
  - Sulfonylurea screen negative
  - CT negative for pancreatic mass
- Because her hypoglycemia was exclusively postprandial, empiric therapy was instituted rather than pursuing invasive testing to rule out insulinoma
- She started a 30-gram per meal CHO restricted diet and initially responded
- However increasing CHO intake resulted in symptomatic hypoglycemia
- Pre-meal AGI therapy of 50mg TID was initiated with meals
- At 3-year follow-up patient denies symptomatic postprandial hypoglycemia except when she omits AGI therapy

Summary of Cases 1, 2, 3 and 4

Table 1

	Case 1	Case 2	Case 3	Case 4
PP* BG nadir (65-99 mg/dl)	42	32	56	50
Insulin (<29.2 ulU/mL)	14.4	16.4	Lab error	46.7
C-peptide ng/ml	4.2	2.8	Lab error	10.6
CT Abdomen	Negative	Not done	Not done	Negative
Treatment	Carb restricted diet & acarbose	Carb restricted diet & acarbose	Carb restricted diet & acarbose	**Carb restricted diet, allergic to acarbose and miglitol
Time of follow-up	4 years	3 years	2 years	6 months

*PP = postprandial following mixed meal (all patients symptomatic)
**Decrease in PP hypoglycemia with AGI therapy but rash required discontinuation

Discussion

- Most recent review of symptomatic hypoglycemia in GB patients has described an incidence between 0.2-6% (2)
- To date 89 cases have been reported (Table 2)

Table 2

	Cases	Mean age (years)	Time of Onset after GB* (months)	Lowest Glucose Value (mg/dl)
Ritz et al	89	44	28.6	41.4 (at time of symptoms)
Current Series	4	43	42	37 (mixed meal nadir)

*GB = roux-en-y gastric bypass

- Although we did not definitively rule out insulinoma, given the response to AGI therapy we elected not to perform other invasive testing on all patients
- Our mixed meal testing confirmed inappropriate hyperinsulinemia in the presence of symptomatic hypoglycemia
- The etiology of GB hypoglycemia remains unclear
- Symptoms from dumping syndrome can mimic post-prandial hypoglycemia
- However, dumping syndrome occurs weeks to months after surgery versus 1-2 year delay in GB hypoglycemia patients
- Some patients were found to have changes in islet cells consistent with noninsulinoma pancreatogenous hypoglycemia (NIPHS) (1)
- However, Meirer et al (3) did not find islet cell hypertrophy or hyperplasia
- Attention has focused on exaggerated secretion of incretins after meal ingestion

Discussion (cont.)

- Glucagon like peptide-1 levels were found to be significantly increased in GB patients with symptomatic hypoglycemia compared to asymptomatic GB patients (4)
- CHO restriction is the first step instituted to treat symptomatic GB hypoglycemia
- Kellogg et al (5) described 10 out of 12 GB patients had complete or partial improvement of symptomatic hypoglycemia with low CHO diet
- Acarbose has been shown to decrease postprandial hyperglycemia after mixed meal testing as well as attenuate the rise in insulin and GLP-1 levels (6)
- Kellogg et al (5) placed 2 patients on AGI therapy after failing low CHO diet therapy with 1 experiencing improvement
- Moreira et al (7) added AGI to verapamil therapy to a single patient with resolution of hypoglycemia
- Hanaire et al (8) reported the use of AGI therapy in a single patient decreased hypoglycemia after an 8 month follow-up

Conclusions

- We are the first to demonstrate the long-term effectiveness of AGI therapy in GB patients with postprandial hypoglycemia who fail dietary carbohydrate restriction

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