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:
  - Experiencing sweating, palpitations, tremor and neuroglycopenic symptoms 2-4 hours postprandial.
  - Documented capillary glucose (BG) of 35-50 mg/dl.
- Symptoms resolved with sodium HCO3.
- 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 u/mL (<29.2 u/mL).
  - C-peptide 4.2 ng/ml (0.8-9.6 ng/mL).
  - Beta hydroxybutyric acid of 0.08 mM/L (0.0-0.42 mM/L).
  - Salbutamol screen negative.
  - GT 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 30g 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.

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).

Case 2

- 49 M with a history of diabetes with poor control on insulin.
- One year post-GB surgery he was switched to a low carbohydrate diet with a goal of 20% protein, 35% fat, and 45% CHO.
- He was asymptomatic but his BG was less than 50 mg/dL 1 hour after breakfast.
- Patient was started on 25 mg of ORam 3 times per day.
- Improvement was noted.
- Taper to 15 mg and then 5 mg.
- Treatment was discontinued.
- Hypoglycemia occurred 2-3 hours after each meal.
- At 3 months follow up patient had resumed his previous diet.

Table 1

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPG</td>
<td>29-39 mg/dl</td>
<td>24-34 mg/dl</td>
<td>29-39 mg/dl</td>
</tr>
<tr>
<td>Insulin</td>
<td>10.4, 12.4</td>
<td>12.4, 12.4</td>
<td>12.4, 12.4</td>
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<tr>
<td>C-peptide</td>
<td>6.2, 8.2</td>
<td>6.2, 8.2</td>
<td>6.2, 8.2</td>
</tr>
<tr>
<td>CT Adipose</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Treatment</td>
<td>Carbohydrate intake &amp; Ag 4t &amp; Ag 5t</td>
<td>Carbohydrate intake &amp; Ag 4t &amp; Ag 5t</td>
<td>Carbohydrate intake &amp; Ag 4t &amp; Ag 5t</td>
</tr>
<tr>
<td>Time of follow-up</td>
<td>4 years</td>
<td>3 years</td>
<td>2 years</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bills</td>
<td>83, 84</td>
<td>75, 76</td>
<td>75, 76</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>66, 67</td>
<td>66, 67</td>
<td>66, 67</td>
</tr>
<tr>
<td>Mean Time of follow-up (months)</td>
<td>7, 8</td>
<td>7, 8</td>
<td>7, 8</td>
</tr>
<tr>
<td>Lowest Glucose Value (mg/dl)</td>
<td>35, 36</td>
<td>35, 36</td>
<td>35, 36</td>
</tr>
</tbody>
</table>

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 who 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.
- Hanrahi 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.

References: