Managing Endocrine Related Issues after Bariatric Surgery

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Bariatric Surgery was Associated with Higher Remission Rate than Usual Care

DM remission = fasting BG <110 mg/dL and no diabetes medications

L Sjöström et al. JAMA. 2014:2297-2304
Postoperative glycemic control

- Goal: HbA1c ≤7%; FBG ≤110 mg/dL and PBG ≤180 mg/dL
- Patients requiring insulin preop: glucose monitoring; SC insulin (basal bolus regimen + correction insulin Q 3-6 h)
- Some evidence for tighter glycemic control (fasting BG <117 mg/dL) 1-2 weeks after surgery can improve remission rate at 1 yr (Fenske et al. Obes Surg 2012)

An Endocrine Society Clinical Practice Guideline 2010
Daily insulin titration schedule in insulin-requiring T2DM after bypass surgery

Start with dose equivalent to the insulin required in the previous 24 h prior to discharge and adjust it daily

<table>
<thead>
<tr>
<th>Self-monitored fasting glucose values</th>
<th>Adjustment of insulin dosage (IU/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥12 mmol/L (220 mg/dL)</td>
<td>6 ↑</td>
</tr>
<tr>
<td>&gt;10 mmol/L (180 mg/dL)</td>
<td>4 ↑</td>
</tr>
<tr>
<td>&gt;8 mmol/L (144 mg/dL)</td>
<td>2 ↑</td>
</tr>
<tr>
<td>≥7 mmol/L (120 mg/dL)</td>
<td>1 ↑</td>
</tr>
<tr>
<td>5.5–6.9 mmol/L (100–120 mg/dL)</td>
<td>No change in insulin dosage</td>
</tr>
<tr>
<td>&lt;5.5 mmol/L (100 mg/dL)</td>
<td>2 ↓</td>
</tr>
<tr>
<td>&lt;4.5 mmol/L (81 mg/dL)</td>
<td>4 ↓</td>
</tr>
<tr>
<td>&lt;4.0 mmol/L (72 mg/dL)</td>
<td>6 ↓</td>
</tr>
</tbody>
</table>

Case 1

- 45 y.o. female underwent RYGB 3 years ago for obesity and had 60% EWL. Had an episode of loss of consciousness when attending church service. Felt weak, shaky and lightheaded. He stood up then fell to the ground. FSBG was 30 in the field. Plasma glucose was normal when arrived at the hospital. Had two other episodes after this but less severe. All occurred 1-3 hours after a meal.
Hyperinsulinemic Hypoglycemia Syndrome (HHS)!
Post-bariatric surgery hypoglycemia

- Occurs 0.5 to 9 yrs (typically 2~3 y) after RYGB
- Symptoms of hypoglycemia 1-3 h after eating
- Moderate to severe hypoglycemia
- Associated with hyperinsulinemia
- Prevalence 0.2-1%
- Described mostly with RYGB
- Can occur after VSG but rare

Cui et al. J Gastrointes Surg 2011
M Salehi et al. JCEM 2014
Diagnosis

• Postprandial hypoglycemia with neuroglycopenia developing >1 year after gastric bypass
• Hyperinsulinemia at the time of hypoglycemia or, after a mixed meal, plasma glucose < 50 mg/dL, and serum insulin >50 uU/L
• Normal fasting glucose and serum insulin
• Spontaneous correction of hypoglycemia

WHIPPLE’S TRIAD!!!
Management of HHS

• Nutritional manipulation:
  – low-carbohydrate diet, avoid sucrose
  – fructose-sweetened foods
  – glucose tablets 60-90 min after a meal or first symptoms of hypoglycemia

• Medical therapy:
  1) Acarbose (25-50 mg TID)
  2) Diazoxide (5-15 mg/kg/d in divided doses)
  3) Octreotide (5-20 mcg/kg/day in divided doses)
  4) Calcium-channel blockers (verapamil or Nifedipine) – not effective

AACE/TOS/ASBMS guidelines 2013 and expert opinions
Management of HHS

- Gastric restriction
- Reversal of bariatric procedure (RYGB to SG)
- Partial or total pancreatectomy – not recommended by some experts
Case 2

- 51 y.o. female underwent RYGB 5 yrs ago for morbid obesity and T2D. C/o hip pain and worsening back pain, difficulty climbing stairs, muscle aches, decreased energy and fatigue.

- PE: BP 140/90, HR 80, Temp 97.5. No point tenderness, full range of motion of joints, muscle strength 5/5.
• Chest X ray: normal.
• CBC: mild iron-deficiency anemia. Chem panel: normal Ca, alk phos, phosphorus. LFTs: WNL.
• 1,25-OH-vitD: 35
• 25-OH-vitD: 9
• DXA: osteoporosis
Prevalence of Vitamin D deficiency

Legend: * p<0.001; OG: operated group; CG: control group

Costa et al. Osteoporos Int 2015:757
VitB1, Ca, iron, copper, zinc, selenium, folate, B12, copper, Vit A, D, E and K (jejunum and ileum)
Pathways of vitamin D synthesis

7-dehydrocholesterol

Diet/supplements

UV light skin

Cholecalciferol (vitamin D3)

Ergocalciferol (vitamin D2)

Liver

Calcidiol (25-hydroxyvitamin D)

Kidney

Calcitriol (1,25-dihydroxyvitamin D)

Inactive metabolite (24,25-dihydroxyvitamin D)

↑ Intestinal absorption of calcium

↑ Bone resorption

↓ Renal Ca++ and phosphate excretion

Metabolic activation of vitamin D to calcitriol and its effects on calcium and phosphate homeostasis. The result is an increase in the serum calcium and phosphate concentrations.

UV: ultraviolet.
The big picture

PARATHYROID GLANDS
- Sense low serum calcium and increase PTH secretion

BONE
- Releases calcium and phosphorus

Increased serum calcium

Vitamin D

Liver
- Calcidiol (25-OH-D)
- Increases calcitriol formation
- Decreases excretion of calcium

Kidney
- Calcitriol (1,25(OH)₂D)
- Increases absorption of dietary calcium

Small Intestine
25-OH-D and Parathyroid hormone

Valcour et al. JCEM 2012:3989
Consequence of VitD deficiency

- Mild to mod: accelerate bone loss – low bone mass on DXA and fractures
- Prolonged and severe: ↓ GI absorption of Ca and Phos → hypocalcemia → secondary HPT → phosphaturia, demineralization of bone, osteomalacia; proximal muscle weakness
- Parathyroid gland hyperplasia and adenoma
- Extra-skeletal effects: immune function, CV and metabolic health, cancer
Treatment of VitD deficiency

- Vitamin D3 (cholecalciferol)
- Vitamin D2 (ergocalciferol)
- Every 100 units of added D3, 25-OHD ↑ by 0.7-1.0 ng/mL (normal absorptive capacity)
- High risk patients with 25-OHD <20 ng/mL: 50,000 IU D2 or D3 1-2 times weekly x 8 wks. 10,000-50,000 IU daily may be necessary for malabsorption
- [http://dminder.info](http://dminder.info) (Dr. Michael Holick)
- Obese patients need 2-3x more D!
Treatment of VitD deficiency

- Those remain deficient –
  - Vitamin D absorption test
  - Confirm low level by liquid chromatography assay
  - UVB exposure: 2-3x/week then 1x/week, cover sensitive areas, sun screen to face
  - VitD metabolites: calcidiol (25-hydroxy D, liver disease), calcitriol (1,25-dihydroxy D, renal failure) – can worsen 25-OH-D deficiency
- Total Ca intake: 1200-1500 mg daily
Thank you!

Questions?