Strike The Spike!

Strategies for Combatting After-Meal Highs

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Overview

- Definitions
- Risks
- Detection
- Management
After-Meal Peaks Defined

The net rise that occurs from before eating to the highest point after eating.

- **ADA Goal:** <180 mg/dl 1-2 hrs after start of meal
- **AACE Target:** <140 mg/dl at “peak”
- **European Diabetes Policy Group:** <165 (to prevent complications)
- **International Diabetes Federation:** <140 mg/dl 2 hrs after meal
After-Meal Goals

• **Children:**
  < 200-240 @ peak
  (< 100 pt. Rise)

• **Adults:**
  < 180-200 @ peak
  (< 80 pt. Rise)

• **Pregnancy**
  < 140-160 @ peak
  (< 60 pt. Rise)
After-Meal Peaks: Reality in Type-1 Diabetes

Source: Boland et al, Diabetes Care 24: 1858, 2001
After-Meal Peaks: Reality in Type-1 Diabetes

Source: Boland et al, Diabetes Care 24: 1858, 2001
After-Meal Highs: Immediate Problems

- Tiredness
- Difficulty Concentrating
- Impaired Athletic Performance
- Decreased desire to move
- Mood Shifts
- Enhanced Hunger
After-Meal Highs: Immediate Problems

Australian Study of Children w/Type 1. Parents & children reported BG > 270 had negative impact on:

- Thinking (68%)
- Mood/Emotions (75%)
- Coordination (53%)

J Pediatr Endocrinol Metab. 2006 Jul;19(7); 927-36
Long-Term Problems

Relative Influence on HbA1c

Source: Monnier et al, Diabetes Care, 26, 3/03, 881-885
Long-Term Problems (contd)

52 Type 1’s, similar BP between groups

<table>
<thead>
<tr>
<th>Post-prandial glucose</th>
<th>Range</th>
<th>Time to onset of proteinuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent &lt;200</td>
<td>110-198</td>
<td>23 yrs</td>
</tr>
<tr>
<td>Intermittent &gt;200</td>
<td>118-228</td>
<td>19 yrs</td>
</tr>
<tr>
<td>Persistent &gt; 200</td>
<td>201 +</td>
<td>14 yrs</td>
</tr>
</tbody>
</table>

Source: Kidney Intl. 1987; 32 (supp 22): S53-S56
Long-Term Problems (contd)

Type-2s Starting on Oral Meds

<table>
<thead>
<tr>
<th></th>
<th>Meds to limit post-meal rise</th>
<th>Meds to control pre-meal BGs</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c reduction</td>
<td>Identical</td>
<td>Identical</td>
</tr>
<tr>
<td>Fasting BG</td>
<td>Identical</td>
<td>Identical</td>
</tr>
<tr>
<td>Cognitive Function</td>
<td>Unchanged</td>
<td><strong>Declined</strong></td>
</tr>
</tbody>
</table>

Source: Neurology 2006; 67: 235-240
Long-Term Problems (contd)

Rates of eye and kidney disease based on glucose variability (using CGM) in Type-2 Diabetes

Source: Liu et al, American Diabetes Association 71st Scientific Sessions 2011, Abstract 2205-PO.
Long-Term Problems (contd)

22-yr CVD Mortality Risk by Baseline post-challenge glucose

Long-Term Problems (contd)

Glycemic Variability A Better Predictor of Major Cardiac Events than Admission BG or A1c for Acute MI (Su et al, Diabetes Care online, 1/24/2013)

1 & 2-Hr. BG levels predicted CHD better than fasting BG (Pyorala et al, J Chronic Dis. 1979; 32, 729-745)

Long-Term Problems (contd)

Post-Lunch BG Linked Strongly to Hazard Ratio for First CV Event
(Ceriello, Intl. Diab. Mon. 2007; 19:2; 33-36)

Post-Brkfst BG predicted mortality better than fasting BG (Hanefeld et al, Diabetologia 1996; 39: 1577-1583)
Long-Term Problems (contd)
Acute Hyperglycemia: Proposed Mechanism of Damage

Source: Antonio Ceriello, Univ. of Udine, Italy. *Diabetes* 54: 1-7, 2005

Coagulation Abnormality
Oxidative Stress
Endothelial Dysfunction
Contribution of endothelial progenitor cells (EPCs)

- Damage to inner lining of blood vessels (endothelium) leads to vascular complications
- EPCs “patch” endothelial injuries
- EPC count increases with reduction in glycemic excursions

Measurement of After-Meal Peaks

- **Fingerstick BG Checks**
  - Capillary (finger) sample
  - Check BG 1 Hr after *completion* of meal
  - (or) every 15, 20 or 30 min until 2 consecutive BG reductions occur (No addl. Food/insulin until test is completed)
# Meter Test Example

<table>
<thead>
<tr>
<th>Breakfast</th>
<th>Lunch</th>
<th>Dinner</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre</strong></td>
<td><strong>1h Post</strong></td>
<td><strong>Pre</strong></td>
</tr>
<tr>
<td>117</td>
<td>281</td>
<td>157</td>
</tr>
<tr>
<td>90</td>
<td>302</td>
<td>58</td>
</tr>
<tr>
<td>151</td>
<td>264</td>
<td>77</td>
</tr>
</tbody>
</table>

**Interpretation:**

Excessive after-meal peak following breakfast; not after lunch or dinner
## Meter Test Example

<table>
<thead>
<tr>
<th>Time pp</th>
<th>BG Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premeal</td>
<td>135</td>
</tr>
<tr>
<td>:20</td>
<td>155</td>
</tr>
<tr>
<td>:40</td>
<td>168</td>
</tr>
<tr>
<td>1:00</td>
<td>214</td>
</tr>
<tr>
<td>1:20</td>
<td>222</td>
</tr>
<tr>
<td>1:40</td>
<td>175</td>
</tr>
<tr>
<td>2:00</td>
<td>141</td>
</tr>
</tbody>
</table>

**Interpretation:**

Peak occurred at 1hr, 20min pp; rise from premeal to peak was approx. 90 mg/dl
Measurement of After-Meal Peaks

- **Blinded CGM**
  - Medtronic iPro (72 hrs) or Blinded Dexcom 7+ (7 days)
  - BG data every 5 minutes
  - Analysis software shows post-meal patterns
Measurement of After-Meal Peaks

• Real-Time Continuous Glucose Monitors

  – Allow tracking of post-meal trends
  – Produce BG estimates every 5 minutes
CGMS Case Study

37 year old man (insulin pump)
CGMS Case Study

8 year old girl (glargine/MDI)
CGMS Case Studies

60-year old woman (oral meds)
Spike Measurement

1,5 – anhydroglucitol (AG) “GlycoMark”

- Laboratory Blood Test
- Measures Duration & Magnitude of High BG Excursions for past 10-14 days
- “Normal” is >14 μg/ml
- >10 is “good”
Why Do We Spike?

• **Insulin/Meds Work Too Slowly**
  – Lag *far* behind pancreatic insulin
  – Glucagon is not properly suppressed

• **Food Works Too Quickly**
  – Lack of amylin hormone
Spike Control

- Make Insulin Work Faster
- Make Food Work Slower
Slowing Food 1: Use of Glycemic Index

- All carbs (except fiber) convert to blood glucose eventually
- G.I. Reflects the magnitude of blood glucose rise for the first 2 hours following ingestion
- G.I. Number is % or rise relative to pure glucose (100% of glucose is in bloodstream within 2 hours)
Example:

Spaghetti

GI = 37

• Only 37% of spaghetti’s carbs turn into blood glucose in the first 2 hours.

• The rest will convert to blood glucose over the next several hours.
Glycemic Index (contd.)

- Lower GI foods digest & convert to glucose more slowly
- High-fiber slower than low
- Hi-fat slower than low
- Solids slower than liquids
- Cold foods slower than hot
- Type of sugar/starch affects GI

- Fastest
  - Glucose
  - Dextrose
  - Starch (branched-chain)
  - Sucrose/Corn Syrup
  - Fructose
  - Starch (straight-chain)
  - Lactose
  - Galactose

- Slowest
  - Sugar Alcohols
## Glycemic Index (contd.)

<table>
<thead>
<tr>
<th>Slow Stuff</th>
<th>Average Stuff</th>
<th>Fast Stuff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasta</td>
<td>Fruit</td>
<td>Breads/Crackers</td>
</tr>
<tr>
<td>Legumes</td>
<td>Juice</td>
<td>Salty Snacks</td>
</tr>
<tr>
<td>Salad Veggies</td>
<td>Pizza</td>
<td>Potatoes</td>
</tr>
<tr>
<td>Dairy</td>
<td>Soup</td>
<td>Rice</td>
</tr>
<tr>
<td>Chocolate</td>
<td>Cake</td>
<td>Cereals</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sugary Candies</td>
</tr>
</tbody>
</table>
## Common Substitutions

<table>
<thead>
<tr>
<th>Meal</th>
<th>High-GI Options</th>
<th>Low-GI Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breakfast</strong></td>
<td>Cereal, Bagel, Waffle, Pancakes, Muffins</td>
<td>Oatmeal, Milk, Whole Fruit</td>
</tr>
<tr>
<td><strong>Lunch</strong></td>
<td>White Bread, Fries, Tortillas, Cupcake</td>
<td>Sourdough/Pumpernickel, Yogurt, Corn, Carrots</td>
</tr>
<tr>
<td><strong>Snacks</strong></td>
<td>Pretzels, Chips, Crackers, Doughnuts</td>
<td>Fruit, Popcorn, Nuts, Ice Cream, Chocolate</td>
</tr>
<tr>
<td><strong>Dinner</strong></td>
<td>Rice, Mashed or Baked Potatoes, Rolls</td>
<td>Pasta, Peas, Beans, Sweet Potato, Salad Veggies</td>
</tr>
</tbody>
</table>
Slowing Food 2: Splitting The Meal

✓ Part at the usual mealtime
✓ Part 60-90 minutes later
✓ Full insulin/meds given prior to meal
Slowing Food 3: Post-Meal Physical Activity

Muscle Use Soon After Eating

- Accelerated Insulin Absorption
- Delayed Digestion
- Glucose Uptake/Utilization

Improved After-Meal Control
Slowing Food 4:
Add Some Acidity

60-min glucose response 55%*

✓ Tomatoes
✓ Sourdough
✓ Vinegar (Salad Dressing/Condiments)

Slowing Food 5: Meal Sequencing

- Eat veggies before starch when having mixed meals
- Make lunch the “higher carb” meal (less at breakfast & dinner)

Slowing Food 6: Medicinal Approaches

α-Glucosidase Inhibitors (acarbose, miglitol)

+ **Slows carb absorption** in the small intestine
+ Gradual glycemic rise post-meal
- Often causes GI upset/flatulence
Medicinal Approaches

DPP-IV Inhibitors:
(sitagliptin, vildagliptin)

+ facilitate glucose-dependent insulin secretion
+ suppress glucose-dependent glucagon secretion
+ slow gastric emptying
GLP-1s (exenatide, liraglutide)

- subcutaneous injectible hormone
+ enhances 1\textsuperscript{st} & 2\textsuperscript{nd} phase insulin secretion
+ slow gastric emptying
+ suppresses appetite
- may cause nausea
Medicinal Approaches

Amylin Analog: (pramlintide)
- subcutaneous injectible hormone
+ enhances satiety
+ slows gastric emptying
+ suppresses post-meal glucagon secretion
- may cause nausea
Effect of Pramlintide on Gastric Emptying in Type 1 Diabetes

Mean Half-Emptying Time (h)

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>~1-h delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>30 µg</td>
<td></td>
<td></td>
<td>*</td>
<td></td>
<td></td>
<td>~1-h delay</td>
</tr>
<tr>
<td>60 µg</td>
<td></td>
<td></td>
<td>*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Breakfast

Single SC pramlintide doses: n = 11, crossover; *P<0.004; \(^{99m}\)Tc labelled pancake; solid component measured
Data from Kong MF, et al. Diabetologia 1998; 41:577-583
Pramlintide Reduces Postprandial Glucagon

Type 2 Diabetes, Late Stage

Type 1 Diabetes

Insulin Sustacal®

Placebo or 100 µg/h pramlintide infusion

Placebo or 25 µg/h pramlintide infusion


Type 2 diabetes, n = 12; AUC₁-₄ h; P = 0.005
Type 1 diabetes, n = 9; AUC₁-₅ h; P < 0.001
Slowing Food 7: Avoiding Pre-Meal Hypoglycemia

Symptomatic hypoglycemia produces “Sieve Effect”

Accelerates gastric emptying of liquids and solids

Produces more rapid BG rise after meal

J Clin Endo Metab 2005; 90: 4489-95
Speeding Insulin 1: Choice of Bolus Insulin

Aspart, Glulisine, Lispro
- 1-hr. peak
- 3-4 hr. effective duration

Vs. Regular Insulin
- 2-3 hr. peak
- 4-6 hr. effective duration
Speeding Insulin 2: Timing of Bolus Insulin
(rapid analog)

<table>
<thead>
<tr>
<th>BG Range</th>
<th>High GI</th>
<th>Moderate GI</th>
<th>Low GI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG Above Target Range</td>
<td>30-40 min. prior</td>
<td>20-30 min. prior</td>
<td>10-15 min. prior</td>
</tr>
<tr>
<td>BG Within Target Range</td>
<td>20-30 min. prior</td>
<td>10-15 min. prior</td>
<td>0 min. prior</td>
</tr>
<tr>
<td>BG Below Target Range</td>
<td>0 min. prior</td>
<td>5-10 min. after</td>
<td>15-20 min. after</td>
</tr>
</tbody>
</table>
Does Timing Matter?

- Bolus w/meal
- Bolus pre-meal
Does Timing Matter?

Note: *Carbs estimated w/pre-meal insulin.*
*Carbs known with post-meal insulin.*

Source: Clinical Therapeutics 2004; 26:1492-7.
Does Timing Matter?

- Insulin taken with meal
- Insulin taken 15-30 min Pre-Meal (if >150)

Speeding Insulin 3: Choice of Insulin Program

**Pump & MDI**
- Meal/snack boluses

**Vs.**

**Daytime NPH**
- Prolonged peak covers midday meals/snacks
Speeding Insulin 4:
Warming The Injection/Infusion Site
Warming The Injection/Infusion Site

“Insupatch” (experimental)

- Heating element in pump infusion site
- Warms site to 38-40°C
- 30-40 minute earlier insulin peak
Speeding Insulin 5: Afrezza

**Graph: Time to Peak Insulin Level**

- Early insulin response in healthy individuals
- AFREZZA™
- Rapid-Acting Analog
- Regular Human Insulin

Data from different studies

2. Insulin Aspart, 0.2 U/kg, Regular Human Insulin, 0.2 U/kg units. Subcutaneous injection in abdomen. Adapted from Mudalier SR et al. Diabetes Care. 1999;22:1501-1506.
Speeding Insulin 6: IM Injection

IM Injection given

![Graph showing the effect of an IM injection on insulin levels over time.]
Meglitinides:
(repaglinide, nateglinide)

+ Stimulates pancreatic insulin secretion
+ **Rapid-acting** (1-2 hour peak)
- ↑ Risk of hypoglycemia
- Must have beta-cell function
# Meglitinide Comparisons

<table>
<thead>
<tr>
<th></th>
<th>Mean max BG at peak</th>
<th>% of time &gt;200 mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repaglinide</td>
<td>210</td>
<td>1%</td>
</tr>
<tr>
<td>Glimepiride</td>
<td>256</td>
<td>5%</td>
</tr>
</tbody>
</table>

Speeding Insulin 8:
Post-Meal Physical Activity

Muscle Use Soon After Eating

- Accelerated Insulin Absorption
- Delayed Digestion
- Glucose Uptake/Utilization

Improved After-Meal Control
Effects of Post-Meal Walking

30 Minutes of casual stop & go walking after meals

✓ Avg. 30 mg/dl (1.75 mmol/L) BG reduction

✓ Peak post-meal glucose 45% higher when not walking

Examples: After-Meal Activity

• Walking Pets
• Household Chores
• Planned Exercise
• Shopping
• Gardening

• Casual Stroll
• Dancing
• Bowling
• Mini Golf
• Skating
“Ze Art of Making Romance”
Summary

After-Meal Blood Sugar Levels Are:

- Important to Control
- Measurable
- Manageable
Post-Meal Mgt Summary

To Slow Food:
1. Choose Low-GI
2. Split Meal
3. Sequence Properly
4. Add Acidity
5. Use $\alpha$Glucosidase Inhibitor
6. Use GLP1/Amylin
7. Post-Meal Activity

To Speed Insulin:
1. Use rapid analogs
2. Pre-Bolus
3. Warm Site
4. Inhaled Insulin
5. Intramuscular Injection
6. Use Meglitinide (oral)
7. Post-Meal Activity
For More Information:

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