Current Strategies for Postprandial Glucose Control

EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be better able to:

1. Describe the pathophysiology of diabetes
2. Describe the use of both fasting glucose and postprandial glucose (PPG) levels to assess glucose control
3. Explain the risks of uncontrolled postprandial hyperglycemia
4. Identify medications that can be used to decrease PPG levels according to the American Diabetes Association guidelines
5. Discuss basic characteristics of currently available medications that target PPG, including mechanism of action, administration, common adverse effects, advantages, and disadvantages
6. Design an evidence-based medication regimen for a patient with postprandial hyperglycemia

Post-Test/Rationale

1. The initial, core pathophysiologic defect of type 2 diabetes is:
   
   A. Beta cell destruction
   B. Decreased glucagon secretion from the pancreas
   C. Increased insulin resistance***
   D. Decreased insulin secretion from the pancreas

Correct answer: C
   
The initial, core pathophysiologic defect in type 2 diabetes is insulin resistance in the muscle, liver, and adipocytes, leading to impaired glucose uptake into cells after meals and increased hepatic glucose output. Early in the disease process, beta cells in the pancreas try to compensate for insulin resistance by increasing insulin secretion.

2. Which of the following statements accurately describes the contribution of fasting plasma glucose (FPG) and postprandial glucose (PPG) to hyperglycemia according to hemoglobin A1C (A1C)?

   A. FPG and PPG contribute equally at all A1C levels
   B. FPG contributes more as the A1C increases***
   C. PPG contributes more as the A1C increases
   D. PPG contributes more at all A1C levels

Correct answer: B
   
The A1C level reflects an average glucose level over a 3-month period with contributions of both FPG and PPG levels. The relative contribution of these components to hyperglycemia varies depending on the overall level of glycemic control. As A1C levels increase, there is more contribution by FPG; as A1C levels approach normal levels, there is more contribution by PPG.
3. Which of the following treatment goals for postprandial glucose (PPG) is recommended by the American Diabetes Association?

A. 1-hour PPG < 140 mg/dL  
B. 2-hour PPG < 140 mg/dL  
C. 2-hour PPG < 180 mg/dL***  
D. 2-hour PPG < 130 mg/dL

**Correct answer: C**
The American Diabetes Association recommends a goal PPG of < 180 mg/dL 1 to 2 hours after meals.

4. Which of the following statements is correct regarding the risks of postprandial hyperglycemia?

A. Postprandial hyperglycemia has been associated with increased cardiovascular mortality***  
B. Fasting plasma glucose is a better predictor of cardiovascular mortality than postprandial glucose (PPG)  
C. Long-term studies have consistently shown that lowering PPG reduces the risk of cardiovascular mortality  
D. Postprandial hyperglycemia does not appear to increase the risk of long-term diabetes complications

**Correct answer: A**
Increasing evidence confirms an independent association between PPG and overall mortality, cardiovascular mortality, heart disease, and microvascular complications. Some data indicate that elevations in PPG may be a better predictor of cardiovascular mortality than fasting plasma glucose elevations. There remains, however, a need for consistent evidence that lowering PPG levels reduces the risk of long term complications.

5. Which of the following medications primarily targets postprandial glucose (PPG)?

A. Glimepiride  
B. Metformin  
C. Pioglitazone  
D. Repaglinide***

**Correct answer: D**
Metformin and pioglitazone primarily target fasting plasma glucose (FPG) and have little direct impact on PPG levels. Sulfonylureas increase insulin secretion and, thus, lower both FPG and PPG indiscriminately, but because of their slow onset of action, they do not impact first-phase insulin secretion. The meglitinides, including repaglinide, have a faster onset and shorter duration of action than sulfonylureas and target PPG.
6. Which of the following medications lowers hemoglobin A\textsubscript{1C} by slowing the rate of carbohydrate absorption in the small intestine?

A. Nateglinide  
B. Miglitol***  
C. Saxagliptin  
D. Dapagliflozin  

**Correct answer: B**  
Miglitol is an alpha-glucosidase inhibitor that lowers postprandial glucose by slowing the rate of carbohydrate absorption in the small intestine. Nateglinide increases insulin secretion from the pancreas. Saxagliptin is a dipeptidyl peptidase-4 inhibitor, which increases physiologic levels of glucagon-like peptide-1 and gastric inhibitory polypeptide, thus increasing insulin secretion and decreasing glucagon secretion. Dapagliflozin is a sodium glucose cotransporter-2 inhibitor and increases urinary glucose excretion.

7. Which of the following statements accurately compares glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dipeptidyl peptidase-4 (DPP-4) inhibitors?

A. GLP-1 RAs are taken by mouth; DPP-4 inhibitors are administered by subcutaneous injection  
B. GLP-1 RAs slow gastric emptying and increase satiety; DPP-4 inhibitors do not slow gastric emptying or affect satiety***  
C. GLP-1 RAs are well tolerated; DPP-4 inhibitors cause gastrointestinal adverse effects such as nausea  
D. GLP-1 RAs are weight neutral; DPP-4 inhibitors cause weight loss  

**Correct answer: B**  
In addition to increasing glucose-dependent insulin secretion and decreasing glucose-dependent glucagon secretion, the GLP-1 RAs also slow gastric emptying and increase satiety, which lead to weight loss. However, there is also an increased risk of gastrointestinal adverse effects such as nausea. GLP-1 RAs are administered as subcutaneous injections, and DPP-4 inhibitors are taken by mouth. DPP-4 inhibitors are weight neutral and they do not contribute to weight loss. Overall, DPP-4 inhibitors are very well tolerated.

8. Compared to regular human insulin, rapid-acting insulin analogs:

A. More closely mimic physiologic prandial insulin secretion***  
B. Are more likely to cause hypoglycemia  
C. Are not recommended by American Diabetes Association guidelines because of their high cost  
D. Have a longer duration of action  

**Correct answer: A**  
Rapid-acting insulin analogs (RAIAs) more closely mimic physiologic prandial insulin secretion than regular insulin because they have a faster onset of action and shorter duration of action.
These pharmacodynamic differences have led to improved hemoglobin A1C levels and fewer episodes of hypoglycemia with RAIAs in some studies. For these reasons, the American Diabetes Association guidelines recommend using RAIAs over regular human insulin.

9. Which of the following glucagon-like peptide-1 receptor agonists (GLP-1 RAs) is categorized as a short-acting GLP-1 RA that primarily targets postprandial glucose (PPG)?

   A. Albiglutide (Tanzeum)
   B. Dulaglutide (Trulicity)
   C. Exenatide (Byetta)***
   D. Liraglutide (Victoza)

**Correct answer: C**
Lixisenatide and exenatide are short-acting GLP-1 RAs with targeted reductions in postprandial glucose (PPG). Albiglutide, dulaglutide, exenatide XR, and liraglutide are longer acting GLP-1 RAs that lower both PPG and fasting plasma glucose.

10. Mr. Parker is a 59-year-old obese man with type 2 diabetes for 12 years. He takes metformin 1000 mg twice daily and insulin glargine 36 units subcutaneously once daily. His hemoglobin A1C (A1C) today is 7.9%. He self-monitors his blood glucose levels in the morning before breakfast. His average fasting plasma glucose (FPG) is 118 mg/dL. Which of the following plans is most reasonable?

   A. Increase insulin glargine to 40 units subcutaneously once daily
   B. Start an alpha-glucosidase inhibitor
   C. Start a sulfonylurea
   D. Start a glucagon-like peptide-1 receptor agonist***

**Correct answer: D**
The patient case illustrates a scenario where the patient has achieved the FPG target of 80 to 130 mg/dL but still has an elevated A1C. The glucose profile abnormality is likely due to increased postprandial glucose (PPG) levels and a medication that targets PPG, offer a low risk of hypoglycemia, and has beneficial effects on weight should be considered. A glucagon-like peptide-1 receptor agonist (GLP-1 RA) is recommended by the American Diabetes Association and the American Association of Clinical Endocrinologists in this situation. Alpha-glucosidase inhibitors lower PPG but have modest impacts on A1C and have high rates of gastrointestinal adverse effects. Sulfonylureas do not specifically target PPG and also cause weight gain and hypoglycemia. The FPG target has been reached, so increasing insulin glargine will not achieve A1C goals and may increase the risk of hypoglycemia.