Emerging Rapid-Acting Insulin Therapies

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 and postprandial glucose levels to assess glucose control;
3. Explain the risks of uncontrolled postprandial hyperglycemia;
4. Identify medications that can be used to decrease postprandial glucose levels per the American Diabetes Association (ADA) guidelines;
5. Discuss basic characteristics of currently available postprandial medications, including mechanism of action, dosage and administration, adverse effects, and drug interactions;
6. Discuss major aspects of postprandial medications that are currently in development, with a focus on rapid-acting insulins; and
7. Design an evidence-based medication regimen for a patient with postprandial hyperglycemia.

Post-Test/Rationale

1. According to recent estimates, approximately how many adults and children in the United States have been diagnosed with diabetes?
   
   A. 6 million  
   B. 10 million  
   C. 15 million  
   D. 22 million***

Correct Answer: D

Recent estimates suggest that, in 2014, approximately 22 million adults and children in the United States had a diagnosis of diabetes.

2. Health care costs for a patient with diabetes are estimated to be how much higher than the costs for an age- and gender-matched individual without diabetes?

   A. It does not cost more  
   B. 1.2 times higher  
   C. 1.5 times higher  
   D. 2.3 times higher***

Correct Answer: D

On an individual basis, health care costs are estimated to be 2.3 times higher for people with diabetes than for age- and gender-matched individuals without diabetes.

3. Which of the following are significant markers of glycemia and a patient’s overall exposure to the dangerous effects of high blood glucose?
A. Pre-meal glucose
B. Post-meal glucose
C. Neither is significant
D. Both A and B are significant***

Correct Answer: D
Health care providers who manage hyperglycemia in patients with diabetes must remain mindful of the impact of not only fasting or pre-meal glucose levels but also postprandial glucose levels on hemoglobin A1c levels. These interrelated factors – pre-meal and post-meal glucose – are both significant markers of glycemia and of the patient’s overall exposure to the harmful effects of hyperglycemia.

4. While patients may test postprandial glucose levels at any time, these levels should definitely be included in a patient’s testing regimen:
   A. When fasting levels are not controlled
   B. When hemoglobin A1c (A1C) is controlled
   C. When preprandial goals have been met and A1C goals have still not been achieved***
   D. When preprandial levels are not controlled

Correct Answer: C
Glycemic goals for most non-pregnant adults with diabetes include an A1C level of less than 7%, a preprandial plasma glucose level of between 80 and 130 mg/dL, and a peak postprandial plasma glucose concentration of less than 180 mg/dL. Postprandial glucose levels should be evaluated when A1C goals are not met after preprandial goals have been reached.

5. What are the 3 rapid-acting insulin analogs that can be used to manage postprandial hyperglycemia?
   A. Insulin glargine, insulin aspart, and insulin degludec
   B. Insulin glargine, insulin aspart, and insulin lispro
   C. Insulin lispro, insulin aspart, and insulin glulisine***
   D. Insulin NPH, insulin glargine, and insulin aspart

Correct Answer: C
Currently, there are 3 rapid-acting insulin analogs on the market in the United States: insulin lispro, insulin aspart, and insulin glulisine.

6. The molecular structures of rapid-acting insulin analogs (RAIAs) are slightly different from native human insulin. These differences result in increased absorption rates of insulin from the subcutaneous depot. Which of the following is true regarding RAIAs?
   A. The molecular differences result in less self-association to the hexameric form
   B. RAIAs tend to remain in the monomeric form
   C. The monomeric form is the one that is primarily absorbed from the subcutaneous depot.
   D. All the above are true***
Correct Answer: D
The structure of each of the RAIA molecules has been slightly modified from native human insulin. Changes in the structure of insulin serve to destabilize or reduce the formation of hexamers and retain insulin receptor affinity and activity. Because of these changes, RAIAs tend to exist in the monomeric form and are absorbed more rapidly than regular human insulin.

7. A recent review of rapid-acting insulin analogs reported that the pharmacokinetic profiles for the 3 currently available insulin analogs were similar but that _______ had a slightly more rapid onset than the other 2 analogs.
   A. None; they were all identical
   B. Insulin glulisine***
   C. Insulin lispro
   D. Insulin aspart

Correct Answer: B
A recent review of the rapid-acting insulin analogs concluded that the pharmacokinetic and pharmacodynamic profiles were similar for the 3 insulins. The review also stated that glulisine had a faster onset of action than the other 2 analogs but that this difference was not of clinical significance in terms of treatment satisfaction, reduced rates of hypoglycemia, or glycemic control.

8. If a patient has an insulin-to-carbohydrate ratio of 1:10, how much rapid-acting insulin is needed to cover the glycemic excursion caused by a meal containing 60 grams of carbohydrates?
   A. 6 units***
   B. 3 units
   C. 2 units
   D. 20 units

Correct Answer: A
If a patient has an insulin-to-carbohydrate ratio of 1:10, he would need 1 unit of rapid-acting insulin for every 10 grams of carbohydrates to cover the glucose excursion secondary to that meal. If he is preparing to consume a meal that contains 60 grams of carbohydrates, he would require 6 units of insulin (60 ÷ 10 = 6 units).

9. The ultra-rapid-acting insulin that is formulated with nicotinomide and arginine is:
   A. Afrezza
   B. FIAsp***
   C. VIAject
   D. Nicotinoject

Correct Answer: B
FIAsp is an ultra-rapid-acting insulin formulation that is currently being investigated by Novo Nordisk. This formulation combines insulin aspart, nicotinomide, and arginine.
10. When studied in patients with type 1 diabetes, the inhaled insulin Afrezza was shown to cause which of the following compared to injected insulin aspart?

   A. Higher hemoglobin A1c (A1C) levels and more hypoglycemia
   B. Lower A1C levels and more hypoglycemia
   C. Lower A1C levels and less hypoglycemia
   D. Higher A1C levels and less hypoglycemia***

Correct Answer: D
Rationale: Compared to injected insulin aspart in patients with type 1 diabetes, Afrezza resulted in inferior A1C control, but it reduced hypoglycemia across all A1C groups.