

Insulin Therapy: The Question This Issue

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Note: The goal of this section of *Insulin* is to provide answers to frequently asked questions regarding insulin therapy in diabetes. Readers are encouraged to submit their own questions by visiting www.InsulinJournal.com or by e-mailing insulin@elsevier.com. One or more questions will be addressed each issue.

Question:

I hear about the basal-bolus concept of insulin therapy all the time. What is this concept, and why should my patients use it? Please explain.

Answer:

The goal of insulin therapy—or, for that matter, any treatment in diabetes mellitus (DM)—is to mimic the normal physiology. Thus, it is important to understand the natural physiology of insulin secretion. The normal human pancreas produces some insulin (basal insulin) all the time (the amount may vary slightly throughout the day). When food is consumed, the pancreatic β -cells respond by producing larger amounts of insulin in a more rapid fashion (bolus insulin). The goal of insulin therapy is to mimic this physiology as closely as possible. Furthermore, the glycosylated hemoglobin level is determined by both fasting and postprandial blood glucose levels. It is therefore important to control both fasting and postprandial blood glucose levels to achieve optimal glycemic control.

As we know, currently available insulin therapies can be broadly divided into short-acting or bolus insulin and long-acting or basal insulin. Premixed combinations of these insulins are also available.

Basal Insulins

The ideal basal insulin should have:

- A fairly flat profile (without a peak)
- A duration of action of ~24 hours
- Minimal interpatient and inpatient variability

Lente and ultralente insulins were withdrawn from the market at the end of 2005. Available basal insulins are as follows:

1. Neutral protamine Hagedorn (NPH) insulin. This preparation has been available for >60 years. It has the drawbacks of having a peak and of significant interpatient and inpatient variability. NPH must be mixed aggressively before injection because it is a suspension. It can be mixed with other insulins in the same syringe, while insulin glargine or detemir cannot be mixed.
2. Insulin glargine. This insulin does not have a significant peak, has much more consistent absorption than NPH, and has a longer duration of action (~24 hours in the majority of patients).
3. Insulin detemir. Launched recently, this insulin has a duration of action and a peak between those of glargine and NPH insulin.

Bolus Insulins

The ideal bolus insulin should have:

- A quick onset of action (10–15 minutes)
- A quick peak
- A short overall duration of action (~4 hours)
- Minimal interpatient and inpatient variability

Available bolus insulins are as follows:

1. Human regular insulin. This insulin has been available for >80 years. It should be administered 30 minutes before a meal.
2. Analogue insulins. These include insulins lispro, aspart, and glulisine. These insulins have a faster onset and a shorter duration of action than human regular insulin. Analogue insulins, even given right after a meal, tend to work better than human regular insulin given right before a meal. The ideal time for administration of analogue insulins is 10 to 15 minutes before a meal.

- Inhaled insulin. This insulin appears to have an onset like analogue insulins but a duration of action like human regular insulin.

In real life, most patients with DM do not inject insulin 15 to 30 minutes before a meal. They inject right before eating and, many times, even after eating. This leads to significant postprandial hyperglycemia, especially with human regular insulin. For all practical purposes, analogue insulins are preferable to human regular insulin. Human regular insulin has served us very well for the past 80 years, but in the author's opinion, it has become an insulin of the past.

Basal-Bolus Insulin Therapy (Intensive Insulin Therapy)

In summary, basal-bolus therapy refers to an insulin regimen in which separate insulins provide the basal and the prandial components. Thus, the patient injects basal insulin once or twice daily and injects bolus insulin with meals.

Typically, patients need half basal and half bolus insulin. Thus, when designing a patient's insulin regimen, consider giving half as basal insulin and dividing the other half into 3 doses (equal or unequal, depending on the patient's meal intake) of bolus insulin with meals.

Question:

Why should a patient agree to inject insulin 4 or 5 times a day?

Answer:

The basal-bolus regimen has several advantages. It is a more physiologic regimen, and it leads to better control. The main reason from a patient's perspective, however, is flexibility, flexibility, and flexibility. A regimen's flexibility is directly proportional to the number of shots required.

This regimen gives patients 2 kinds of flexibility. First, it gives them the flexibility of *time*. If patients eat earlier or later, they can inject their bolus insulin earlier or later. This is not true with NPH or premixed-based regimens; with those, when a patient's lunch is delayed, he or she is likely to have hypoglycemia.

This regimen also gives patients flexibility in *meal size*. Patients can inject less or more bolus insulin depending on the amount of food they eat. Human beings tend to eat different amounts at different times. Thus, a patient following a regimen based on fixed bolus doses is not likely to achieve good glycemic control compared with one following a regimen in which the dose can be changed based on meal size.

Question:

What is carbohydrate (carb) counting, and why should my patient with DM do it?

Answer:

Carbohydrate (carb) counting refers to the idea of estimating the expected number of grams of carbohydrates a patient is likely to ingest. One carbohydrate choice, or 1 carb, is equal to 15 g of carbohydrates. Patients either count in terms of grams of carbohydrates or carbs (carb choices). Patients then divide the total grams of carbohydrates by their predetermined compensation factor (see below) to calculate the dose of bolus insulin. Sometimes, if a patient cannot predict how much he or she is going to eat, he or she can take the bolus analogue insulin right after the meal. As mentioned above, this regimen provides more flexibility and better control.

Question:

How do I determine the ratio (compensation factor) that the patient should use?

Answer:

The author recommends the well-known "500 rule" for determining the ratio. Divide 500 by the total daily insulin dose (current total daily dose or dose expected based on weight) to find the number of grams of carbohydrates for which 1 U of insulin can compensate. For example, if a patient has been taking ~50 U of insulin a day, his or her ratio, or compensation factor for carbohydrates, would be 10 (500 divided by 10 = 50), and he or she would inject 1 U of bolus insulin for every 10 g of carbohydrates.

It takes time and effort to learn carbohydrate counting, and the author stresses to patients the importance of carbohydrate counting. Patients should pay close attention during the first few months; the more attention they pay, and the more effort they put in, the better their glycemic control will be for the rest of their life.

Summary:

- The goal of any treatment in DM is to mimic normal physiology by covering both basal and bolus needs.
- Analogue bolus insulins are preferable to human regular insulin for most circumstances.
- The basal-bolus regimen has several advantages, including the flexibility of *time* and *meal size*.
- The more attention and effort patients give to carbohydrate counting, the better their glycemic control will be.