What Do You Need to Know About Traditional Insulin Formulations?

Kim A. Carmichael, MD—*Series Editor*

Q. What is the history and prevalence of insulin use in the United States, and where are we going?

A. Insulin was first isolated and extracted in 1921 and has been available since 1925.[1] Since then, substantial progress has been made in insulin preparations, from early animal insulins, to human insulins in the 1980s, to insulin analogues.[2] Novel insulin analogues continue to develop, with improving profiles in insulin administration and action, as discussed in a previous "Diabetes Q&A" column in *Consultant*.[3]

Between 2014 and 2019, the average price of insulin reportedly increased by 55%.[4] In the past few decades, the market has seen development of ultra-long-acting and ultra-fast-acting insulins, designed to more closely mimic pancreatic β-cell insulin secretion. Although in many respects these products provide better lifestyle flexibility for patients, they are also much more expensive, even when some manufacturers have offered to provide "generic" alternatives and other incentives for lower pricing. There have been multiple governmental efforts to reduce the out-of-pocket expenses for patients, but the base prices may still be reflected in insurance maximums and deductibles. Health care providers therefore need to better understand how to begin therapy or even convert patients back from these newer insulins to more traditional products, such as regular insulin and NPH insulin.

Q. What are the price differences between the newer insulins and the more traditional insulins?

A. Price comparisons are generally based on single-unit dosing, although traditional insulins may need more frequent administration, requiring greater usage of needles and/or syringes. One unit of insulin is defined as the amount needed, on average, to lower the blood glucose level by 50 mg/dL.[4] The traditional insulins as of 2019, cost $0.09 to $0.19 per unit in vials (total, $93-$185) for regular, $0.09 to $0.18 per unit for NPH vials (total, $92-$183), and $0.39 per unit ($117 per 3 mL) in pens. ReliOn brand (regular, NPH, and 70/30) may cost much less ($0.025 per unit; total, $24.88 per vial), and the pen formulation may be purchased for $42.88 (15 mL, $0.03 per unit).[6]

The newer rapid-acting insulins, as of 2019, cost $0.18 to $0.36 per unit (total, $180-$362) in vials, $0.24 to $0.48 per unit (total, $72-$143) in pens, and $1.11 per unit in inhaled cartridges (total, $4.42 per 4-unit cartridge). The long-acting insulins range from $0.34 to $0.42 per unit (total, $340-$417) in vials and $0.27 to $0.41 per unit (total, $81-$248) in pens.

Q. What are the major considerations in transitioning between different insulin products?

A. The major considerations in giving insulin include the onset of action, the peak time that the insulin has maximum strength in lowering the blood glucose level, and total duration of action.[5] Among the relatively newer products, rapid-acting insulins often begin working within about 15 minutes, peak in 1 to 2 hours, and last 2 to 4 hours. Long-acting insulins reach the bloodstream after several hours, and their effects last about 24 hours. Ultra-long-acting insulins begin working in about 6 hours, do not peak, and last 36 hours or more. Among the more traditional insulins, short-acting (regular) insulin starts working in about 30 minutes, peaks in 2 to 3 hours, and lasts 3 to 6 hours. Intermediate-acting insulin (NPH) starts in 2 to 4 hours, peaks in 4 to 12 hours, and lasts 12 to 18 hours.

For the basal insulins, transitioning from long-acting to ultra-long-acting ordinarily requires increasing from one shot daily to at least twice daily, with adjustments in timing. For example, if a patient who is prone to having overnight hyperglycemia is taking glargine or detemir at bedtime to minimize this "dawn phenomenon," then a larger dose of NPH may need to be given at bedtime, with an additional lower daytime dose given before the breakfast meal. In contrast, if the individual is prone to having higher bedtime values with lower glucose levels during the night, the glargine or detemir may have been prescribed to be given with

Continued on page 17

AFFILIATION:
John T. Milliken Department of Medicine, Division of Endocrinology, Metabolism, and Lipid Research, Washington University School of Medicine, St Louis, Missouri

CITATION:
Carmichael KA. What do you need to know about traditional insulin formulations? *Consultant*. 2020;60(11):14, 17. doi:10.25270/con.2020.11.00002

DISCLOSURES:
The author reports no relevant financial relationships.

CORRESPONDENCE:
Kim A. Carmichael, MD, Professor of Medicine, John T. Milliken Department of Medicine, Washington University School of Medicine, 660 S Euclid Ave, St Louis, MO 63110-1010 (carmichaelk@wustl.edu)

Diabetes Q&A *Continued from page 12*

breakfast. In this circumstance, transitioning to twice-daily NPH would likely require that the evening dose be timed closer to the dinnertime meal.

The ultra-long-acting insulins often do not depend on the timing of dosing, but changing to NPH would necessitate closer attention to the individual's daily patterns. Due to the long half-lives of these insulin types, however, the recommended dosing adjustment interval may be 3 to 4 days,[1] so the transition to NPH may require frequent changes during the first 1 to 2 weeks.

Transitioning from the rapid-acting insulins to traditional short-acting insulins may also require adjustments in timing. First, patients need to be aware of the longer duration of the short-acting insulins in order to avoid making adjustments in doses more frequently than about every 6 hours. Otherwise, there can be "dose-stacking" with resultant hypoglycemia. Second, patients may need to time their mealtime dosing to about 30 minutes before eating so that the insulin will be active during nutrient absorption. Individuals with gastroparesis, however, may have longer transit durations, which will also require changes in the timing of mealtime insulin.

For some patients who are resistant to taking more than 2 shots daily, or who do not need intense management, using the traditional insulins in a 70/30 formulation (70% NPH premixed with 30% regular) may be considered, generally given about 30 minutes before the breakfast and dinnertime meals.

SUMMARY

Although insulin analogues show noninferiority to conventional insulins in regard to glycemic control and hemoglobin A_{1c} reductions,[3] they are significantly more expensive, and health care providers need to better understand how to transition some patients back to more affordable options. Newer long-acting and ultra-long-acting insulins allow for more flexibility in timing of insulin administration compared with the traditional NPH basal insulin. The newer ultra-long-acting basal options even have a lower risk of hypoglycemia compared with the newer long-acting insulins.[3] Changing to more-traditional forms of basal insulins would therefore require close attention and adjustments to provide a reasonable margin of glycemic safety. ■

REFERENCES:

1. Meneghini L. New insulin preparations: a primer for the clinician. *Cleve Clin J Med*. 2016;83(5 suppl 1):S27-S33. doi:10.3949/ccjm.83.s1.05
2. Mathieu C, Gillard P, Benhalima K. Insulin analogues in type 1 diabetes mellitus: getting better all the time. *Nat Rev Endocrinol*. 2017;13(7):385-399. doi:10.1038/nrendo.2017.39
3. Hollar L, Carmichael KA. What do you need to know about the newer insulin analogues? *Consultant*. 2019;59(1):18-19. Accessed October 16, 2020. https://www.consultant360.com/article/consultant360/diabetes/what-do-you-need-know-about-newer-insulin-analogues
4. Lee B. How much does insulin cost? Here's how 23 brands compare. GoodRx. August 23, 2019. Accessed October 16, 2020. https://www.goodrx.com/blog/how-much-does-insulin-cost-compare-brands/
5. Insulin Basics. American Diabetes Association. Accessed October 16, 2020. https://www.diabetes.org/diabetes/medication-management/insulin-other-injectables/insulin-basics
6. Fennel D. ReliOn insulin for $25 a vial at Walmart. Diabetes Self-Management. May 1, 2019. Accessed October 16, 2020. https://www.diabetesselfmanagement.com/blog/relion-insulin-for-25-a-vial-at-walmart/