Insulin analogs have made a dramatic entrance into the diabetes management armamentarium. Most attention has focused on short-acting insulin analogs. Recently, a new long-acting insulin analog, glargine (Lantus), has been introduced for patient use.

Both of the patients presented in this article have type 1 diabetes. Case 1 demonstrates the conversion from twice-daily ultralente to glargine. The patient in Case 2 had a significant allergic reaction to previous insulin therapy. She was converted from seven doses a day of lispro to a basal-bolus therapy using glargine and lispro. The considerations related to dosing and the key points for patient education are similar for patients whether they have type 1 or type 2 diabetes.

Case Presentation

Case 1
R.L. is a 66-year-old man who has had type 1 diabetes for 32 years. He has been on a basal-bolus regimen for 6 years using lispro and ultralente. He has had widely fluctuating blood glucose levels including significant hypoglycemia, and he has hypoglycemia unawareness. He is only diabetes complication is diabetic gastroparesis.

His glargine dose was determined by decreasing by 20% his total ultralente dose of 32 units split into breakfast and bedtime doses. He took lispro after meals instead of the more common pre-meal dosing because of his gastroparesis. His lispro doses (12 units after breakfast, 10 units after lunch, and 10 units after dinner) were unchanged with initiation of glargine.

Because R.L. was on twice-daily ultralente and had already taken his morning dose, he was instructed to use about half of the glargine dose on the first night (12 units). He began taking the full prescribed dose of 25 units of glargine on the second night.

R.L.’s blood glucose levels for the first day were: fasting, 99 mg/dl; 2-h postprandial breakfast, 124 mg/dl; 2-h postprandial lunch, 146 mg/dl; and bedtime, 80 mg/dl. Needless to say, he was delighted.

Unfortunately, he has not maintained this level of control over the past month. His already elevated stress level was challenged even further when his wife was diagnosed with breast cancer. One month after starting glargine, his doses were increased to 14 units of lispro after breakfast, 12 units of lispro after lunch, 12 units of lispro after supper, and 34 units of glargine at bedtime to reduce his overall blood glucose average of 216 mg/dl.

The conversion from ultralente to glargine was done without difficulty. R.L. has not had the significant hypoglycemia that he experienced with ultralente. In the past 30 days, he has not experienced any blood glucose levels <50 mg/dl, which were common before the conversion.

Case 2
M.S. is a 22-year-old woman who has had type 1 diabetes for 11 years. She developed an allergic reaction to her insulin within 1 month of starting a regimen of NPH and regular insulin before breakfast, regular insulin before supper, and NPH at 10:00 p.m.

Even after changing insulin brands, she continued to exhibit a site reaction (burning and redness) as well as upper respiratory symptoms. She had a known history of allergies. Diphenhydramine four times a day was initiated but provided no relief of symptoms.

M.S. entered the hospital in May 1989 for desensitization to NPH insulin. The desensitization was unsuccessful, and within 2 months, she had re-developed hives at the injection site and persistent upper respiratory symptoms. From autumn 1989 to 1995, she was on four shots of buffered regular insulin along with daily allergy treatment with an anti-histamine.

In 1995, she was diagnosed with Reynauld’s Syndrome. An angiotensin-converting enzyme (ACE) inhibitor was started to alter the proteinuria noted at that time.

M.S.’s insurance did not allow her to continue her care with the endocrine specialist. From 1995 to May 2000, she was followed by a primary care physician. She returned to the specialist practice in May 2000 on seven daily injections of regular pork insulin. Her glucose control was acceptable with an HbA1c concentration of 7.2%.

M.S. returned to our practice with the concern that she would be unable to continue to obtain pork insulin. In addition, she was very tired of seven daily injections, including a 3:00 p.m. and a 3:00 a.m. injection. Considering the time action of regular insulin, we were concerned with the overlap of the regular insulin. At her first visit back to our office, we discussed the option of glargine accompanied by pre-meal doses of rapid-acting insulin rather than short-acting insulin; however, glargine was not yet available.

Because of our concern with the overlap of the regular insulin, M.S. was changed to lispro. Even with lispro, she developed redness and burning at the injection site. She had maintained her HbA1c in the 7.5% range. Seven daily injections followed...
by seven meals had been a limiting factor in her life as an employed, full-time college student. She had not slept through the night since 1995.

M. S.’s total daily dose of lispro had been 72 units per day. In order to calculate the dosages needed for the new regimen, her total dose was reduced by 20%. The basal-bolus method was used to calculate the doses, assigning 50% of her total dose for her basal insulin. She was instructed to start with 25 units of glargine at bedtime. Based on her body weight and her previous insulin total dose, she was advised that she likely would require as much as 30 units of glargine at 10:00 p.m. Her meal doses of lispro were calculated at ~15–18% of her total dose per meal. She began on 10 units of lispro before breakfast, 8 units of lispro before lunch, and 12 units of lispro before dinner.

Because of her allergy history, she was given a test dose of 5 units of glargine in our office with emergency precautions in place. After 1 hour, she had no burning or site reaction with the test dose.

M. S. has now been on glargine for more than 1 month without any sign of allergic reaction. She has commented that she now has her life back. “I didn’t realize how much I was eating for my insulin,” she said.

“I truly feel free.” She has had consistent fasting blood glucose levels of <120 mg/dl.

Discussion

These two cases illustrate some of the advantages that can accrue by using glargine, the new peakless basal insulin, in a multi-dose regimen. Our clinic was involved in three of the clinical trials associated with the Food and Drug Administration new-drug application for glargine. However, our experiences in using glargine in non-study patients are expanding our knowledge about the day-to-day uses of this new therapy. As with any new diabetes therapy, it is the real-life use by people with diabetes and observations by health care practitioners that truly elucidate how a new product will contribute to improving glucose control in safe and effective ways.

Converting a patient to glargine must be done with caution. Experience has shown that in patients with previously well-controlled diabetes, switching to glargine may lead to significant hypoglycemia unless dosages are reduced appropriately. However, glargine has been associated with less hypoglycemia than NPH insulin in both type 1 and type 2 diabetes.1,2

Patients must receive appropriate instructions and must be followed closely and frequently during the first few weeks after conversion. Interestingly, most of our patients when converted to the new regimen have done so well that they have required little follow-up.

When converting to glargine from ultralente, practitioners must give careful consideration to the long-acting depot effect of ultralente. If an individual is on twice-daily ultralente, the recommendation is to give one-third to one-half of the total dose calculated for glargine on Day 1 and a full dose on Day 2. Practitioners must also give careful consideration to the long duration of action and greater intersubject variability of ultralente compared to NPH.3

Glargine is a peakless insulin with 24-h duration, making once-daily dosing feasible. Based on the NPH comparison trials, bedtime dosing of glargine is recommended.2 Injected into different sites, glargine showed no differences in absorption and very little intrapersonal day-to-day variation in absorption.3

A dietitian should carefully review and monitor food intake during the conversion period. Consistent carbohydrate and calorie intake helps to stabilize glucose levels.

Practitioners and people with diabetes may have to alter their views about snacks. Snacks that were previously needed to prevent low blood glucose levels with intermediate- or long-acting insulin may now cause elevated fasting or pre-meal blood glucose levels. Snacks now become optional based on exercise.

Postprandial blood glucose monitoring can help to determine the effects of rapid- or short-acting insulin. Postprandial blood glucose patterns are used to adjust previous meal insulin doses.

A diabetes educator must provide self-management education about glargine. Patients should be instructed to call, fax, or email their blood glucose levels every 2 or 3 days and should be reminded about how to reach their diabetes care provider 24 h a day in the event of an emergency.

Most patients who respond well to glargine achieve their blood glucose goals within 1–2 weeks after converting to glargine.

Educational Considerations for Patients Switching to Glargine

Glargine cannot be mixed with any other insulin. The pH of glargine is 4.0. If mixed with other insulins, it may cause precipitation and lead to deterioration in glucose control. Consequently, glargine syringes should not be reused for any other insulin. Syringe reuse for glargine alone should follow American Diabetes Association guidelines.4

The acid pH of glargine may cause a slight sting at the injection site. This has been reported to dissipate momentarily.5

Glargine is a clear, long-acting insulin. Its bottle is a taller, thinner 10-ml vial with lavender banding and labeling. Educators must work closely with patients to ensure that they recognize the vial shape, color coding, and other identification differences to prevent medication errors.

If patients have a tendency to confuse their vials of “clear” insulin, it would be clinically acceptable to take the glargine as a morning injection so that any errors would become evident during waking hours.

If patients miss their bedtime basal dose of glargine, clinical experience suggests giving half of the glargine dose for the next morning dose, and the remaining half of the dose that night, and the full dose the next night.

Consistency in carbohydrate and calorie intake is particularly important during titration of glargine doses. Because there is no insulin peak, patients are likely to need less food at bedtime. Individuals can check their blood glucose at 2:00 or 3:00 a.m. to determine whether the glargine needs to be adjusted or less food is needed.
at bedtime. Rapid-acting insulin may need to be given with snacks.  

Careful monitoring of postprandial blood glucose levels after administration of rapid-acting insulin doses is critically important because the introduction of the background glargine may necessitate a reduction in the doses of rapid-acting insulin. The recommended testing frequency is four times per day at fasting and 2 h post-meals. Fasting blood glucose levels should be normalized first, with a goal of 70–130 mg/dl. The target for the 2-h postprandial level is <150 mg/dl.6

Additional food or decreased insulin may be needed for additional exercise. Planned long-duration exercise, such as a ski trip, may require a reduction in glargine dose the day before the trip. Unplanned exercise may require a decrease in the rapid-acting insulin dose and/or increased calories.

Patients should be encouraged to not over treat hypoglycemia. Without a peak, glargine appears to require a smaller amount of oral treatment. Longer-acting foods, such as protein, may not be necessary as a follow-up treatment. Patients need to be encouraged to recheck their blood glucose levels every 15 min after treating hypoglycemia until they have achieved an acceptable glucose level.

Summary
A single injection of basal insulin with insulin boluses for meal coverage mimics physiological insulin secretion. Early clinical experience with glargine has shown improved blood glucose control, particularly of the fasting glucose levels, in many cases. Additionally, there is less likelihood of hypoglycemia, especially nocturnal hypoglycemia, with glargine than with more traditional basal insulins. Like all diabetes therapies, the use of insulin glargine requires a team approach, with patients playing a central role on their team.

References


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Notes of disclosure: Dr. Guthrie, Ms. Hinnen, and Ms. Childs have received honoraria for speaking engagements and consulting fees from Aventis Pharmaceuticals, which manufactures glargine. Dr. Guthrie serves on the Aventis speaker’s panel and has been a principal investigator for several Aventis-sponsored glargine studies. MidAmerica Associates, which employs Ms. Childs and Dr. Guthrie, has received research support from Aventis and Hoechst Marion Roussel for the study of glargine.