Premeal Oral Insulin Rivals the Injectable Form

BY MIRIAM E. TUCKER
Senior Writer

TORONTO — A formulation of insulin that is sprayed in the mouth and absorbed buccally appears to control glucose as well as injected insulin when used before a meal, Dr. Gerald Bernstein reported at the joint annual meeting of the Canadian Diabetes Association and the Canadian Society of Endocrinology and Metabolism.

The product, Generex Oral-lyn, is made by Toronto-based Generex Biotechnology. When sprayed into the mouth using the company's "RapidMist" device, the insulin is absorbed into the buccal epithelium and is dispersed directly into the vascular system, thereby avoiding the problem of digestion that would occur if insulin were swallowed. The product has been approved for use in Ecuador for patients with type 1 and type 2 diabetes, according to a company statement.

Dr. Bernstein, the company's vice president for medical affairs, presented a 3-month interim analysis of a 6-month study conducted by Dr. Jaime Guevara-Aguirre and his associates at the Institute of Endocrinology IEMYR in Quito, Ecuador. A total of 24 adolescents (mean age 15 years) and 5 young adults (21 years) with type 1 diabetes were first stabilized for 6 weeks with basal twice-daily glargine and premeal injections of regular insulin. For the next 6 weeks, they took Oral-lyn immediately before and immediately after lunch instead of the injected regular insulin, while continuing to inject the glargine twice daily and the regular insulin before breakfast and dinner.

At baseline, the group had a mean hemoglobin A_{1c} of 9.9% and mean glucose of 236.6 mg/dL. After stabilization, their mean A_{1c} level dropped to 8.4% and mean glucose—measured by the patients six times each day—dropped to 140.4 mg/dL.

After 3 weeks of substituting Oral-lyn for regular insulin at lunch, the mean A_{1c} was 8.5%, and mean glucose was 143.3 mg/dL. Three weeks later (study week 12), the mean A_{1c} was down to 8.0%, Dr. Bernstein reported.

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Doses of the glargine and the prelunch Oral-lyn were split in this study because previous data on each had shown that doing so improves efficacy. However, in practice, patients could take the entire dose of Oral-lyn prior to the meal, since the timing of its action is similar to that of currently available short-acting analogs: It begins working within 5 minutes, peaks at 30 minutes, and is cleared from the bloodstream by 2 hours, he explained.

A larger study is now underway comparing glargine plus either regular insulin or Oral-lyn given before each meal.

Generex Biotechnology plans to file a submission for approval in Canada and Europe concurrently within the next 12-15 months. Submission to the Food and Drug Administration is expected to follow and may fall within an 18-month time frame, according to a company spokesperson. ■

Glucose, Lipid Testing Advised Postpartum in GDM Women

BY MIRIAM E. TUCKER
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TORONTO — Postpartum testing in women who had gestational diabetes during pregnancy should include both an oral glucose-tolerance test and a lipid profile, Genevieve Dubé and her colleagues advised in a poster presented at the joint annual meeting of the Canadian Diabetes Association and the Canadian Society of Endocrinology and Metabolism.

Data from a retrospective analysis of 223 women with gestational diabetes mellitus (GDM) during pregnancy revealed that postpartum glucose-tolerance abnormalities were common, affecting one-fourth of all women. Moreover, "isolated fasting glucose testing would have failed to identify most cases of postpartum dysglycemia," noted Ms. Dubé, a dietician, and her colleagues at the Centre Régional du Diabète de Laval (Que.). The data also suggested that a lipid profile should be part of the assessment, because many of the women with previous GDM—including those with normal postpartum oral glucose-tolerance test (OGTT) results—have altered lipids suggestive of features of the cardiometabolic syndrome, they said.

The 223 women had received prenatal care between June 2004 and April 2005 at Laval's diabetic pregnancy clinic, where a program of routine postnatal GDM follow-up has been in place since 2002. The group had a mean age of 31 years and a mean body mass index of 28.3 kg/m^2. Two-thirds of the women were white. Insulin treatment was used by 34% during pregnancy. All were told to return at 2 months—whether or not they were still breast-feeding—for postpartum lab testing, which included a 12-hour fasting glucose, a 75-g OGTT, a lipid profile, and a thyroid-stimulating hormone test. A total of 74% (165 patients) showed up, at a mean of 3 months following delivery.

Of the 164 who underwent the OGTT, some form of impaired glucose tolerance was detected in 25% (41 patients), including frank type 2 diabetes in 4% (7 patients), isolated impaired glucose tolerance in 16% (26 patients), isolated impaired fasting glucose in 2% (3 patients), and both impaired glucose tolerance and impaired fasting glucose in 3% (5 patients).

Whatever fasting blood glucose (FBG) cutoff was used, more than half of dysglycemic women would have been missed if screening included only FBG. Among the 41 women with abnormal 2-hour OGTT results, just 49% had FBG values at or above 5.6 mmol/L, 41.5% had FBG levels of 5.8 mmol/L or higher, and 32% had FBG levels of 6.1 mmol/L or higher.

The need for insulin therapy and a first-trimester FBG above 6.1 mmol/L were the only risk factors that significantly predicted postpartum abnormal OGTT, with odds ratios of 1.89 and 3.41, respectively. Maternal age, BMI, parity, macrosomia, and nonwhite race were not predictive. Among the 165 women who underwent postpartum lipid tests, 70% had at least one abnormality, defined as a triglyceride level of 1.7 mmol/L or higher, HDL cholesterol level at or lower than 1.3 mmol/L, or a total cholesterol/HDL cholesterol ratio of 5.0 or greater. Cardiometabolic risk factors were not limited to those with abnormal OGTT results and diabetes. Two-thirds of the 123 women with normal postpartum glucose tolerance had at least one lipid abnormality; 23% had triglyceride levels of 1.7 mmol/L or higher, and 23% had HDL cholesterol of 1.3 mmol/L or lower. Only when those two abnormalities were combined was there a significant correlation with OGTT results.

Although it may be good to bring women in for postpartum testing while they're breast-feeding in order to avoid loss to follow-up, lactation can mask some lipid and glucose abnormalities, she noted. ■