**Pramlintide Equals Meal Insulin, Curbs Side Effects**

**By Sherry Boschert**  
San Francisco

SAN FRANCISCO — Adding an injection of pramlintide at mealtime to basal insulin therapy worked as well as mealtime rapid-acting insulin to control post-prandial glucose levels, but caused less weight gain and hypoglycemia, a study of 112 patients with type 2 diabetes found.

The randomized, open-label, 6-month trial showed that 30% of 56 patients in the pramlintide group and 11% of 56 patients in the rapid-acting insulin group achieved the primary composite end point of a hemoglobin A1c (HbA1c) level of 7% or lower, no increase in body weight, and no severe hypoglycemia, a difference that was significant, Dr. Matthew Riddle of the Oregon Health and Science University, Portland, reported at the annual scientific sessions of the American Diabetes Association.

A prior study by Dr. Riddle and his associates suggested patients with type 2 diabetes on basal insulin glargine could get good postprandial glucose control and HbA1c levels by adding mealtime pramlintide without penalizing insulin, and without weight gain (Diabetes Care 2007;30:2794-9).

The current study enrolled adults with type 2 diabetes who had baseline HbA1c levels of 7%-10%, were on any combination of oral diabetes medications (metformin, sulfonylureas, or thiazolidinediones), and 1 or 2 insulin injections needed, with a fasting plasma glucose goal of 70-100 mg/dL. The pramlintide group started pramlintide (120 mcg before major meals) on day 1 and could titrate down to 60 mcg if needed because of nausea. The rapid-acting insulin group used basal insulin alone for 4 weeks to decrease the risk of insulin-induced hypoglycemia, then added rapid-acting insulin (5 U with major meals).

By week 24, a baseline average HbA1c level of 8.3% in each group had decreased by 0.9% in the pramlintide group and by 1.1% with rapid-acting insulin. In the pramlintide group, 43% of patients reached an HbA1c level of less than 7%, and 29% reached levels below 6.5%, compared with 35% and 32%, respectively, in the rapid-acting insulin group. The differences were not statistically significant in the intent-to-treat analyses.

After 6 months, patients in the rapid-acting insulin group stopped pramlintide because of nausea. Dr. Riddle also has been an adviser and consultant and has received research support from Eli Lilly & Co., Novo Nordisk Inc., and Sanofi-Aventis, which also make insulin and oral glucose control agents.

**Population Screens for Type 2 Do Not Cut Mortality Rates**

**By Robert Finn**  
San Francisco

SAN FRANCISCO — A population-based screening program for type 2 diabetes mellitus (diabetes) comes within historical practice in diabetes-related mortality, according to a large randomized controlled trial presented at the annual scientific sessions of the American Diabetes Association.

Moreover, screened patients offered intensive diabetes treatment did not better in terms of mortality than did screened patients offered routine diabetes treatment, said Dr. Justin Basile Echouffo-Tcheugui of the University of Cambridge (England).

The results call into question the value of large-scale screening for type 2 diabetes and of intensive diabetes management. And they conflict with mathematical models that predicted such screening would result in a 2%-40% reduction in diabetes-specific mortality, he said.

The 79,085 people who participated in the study were at 32 primary care practices in England. Using data from medical records, researchers calculated patients’ Cambridge Risk Score (CRS), which reflects an individual’s risk of developing diabetes. Of the original cohort, 19,981 people with CRS scores above 0.17 were included in the study. According to an earlier study, using a CRS score of 0.17 as a cut-off point results in a 70% sensitivity and a 64% specificity in identifying patients at high risk of type 2 diabetes (Diabetes Care 2002;25:998-8).

In five of the practices, having a total of 4,137 high-risk patients, no further screening was offered. These patients constituted the control group. In the remaining 27 practices, patients were offered stepwise screening for type 2 diabetes.

In the first step, the test used was a glucose tolerance test for a definitive diagnosis of diabetes.

In 13 practices, with 7,462 high-risk patients, those with diabetes were offered intensive care. In the practices, with 8,282 high-risk patients, those with diabetes were offered intensive treatment. In all, 78% of the high-risk patients in the routine care and intensive care practices attended thestepwise screening, and 407 received a diagnosis of diabetes. During 104,218 person-years of observation (a mean of 5.5 years of follow-up per patient), there were 744 deaths in the screening practices and 192 deaths in the control practices.

After adjusting for the practice, age, gender, and asthma and antihypertensive drugs, the researchers found no significant differences between patients in screening practices and those in control practices in overall mortality, cardiovascular mortality, or cancer mortality. There were also no significant differences between the intensive care and routine care patients in overall, cardiovascular, or cancer mortality.

There were two positive results in the trial. In screening practices, high-risk patients who agreed to be screened had an 86% higher overall mortality than those in the control practices. Those with an HbA1c level above 7.5%,” Dr. Yossef C. Blum said during a poster session at the annual meeting of the American Academy of Orthopaedic Surgeons.

In a review of inpatient and outpatient charts of total knee or hip arthroplasty performed by a single surgeon at one institution from 2000 to 2007, Dr. Blum, of Montefiore Medical Center, New York, and his associates found 199 patients whose HbA1c level had been measured in the year before surgery or within 3 months after the surgery. Those with conditions other than diabetes that led to an immunosuppressed state, such as HIV or rheumatoid arthritis, were excluded.

Patients did not have to have a diagnosis of diabetes to be included—just an HbA1c measurement because up to a third of people with diabetes do not have a formal diagnosis, they reported.

In all, 73% of the patients underwent total knee arthroplasty and 27% had total hip arthroplasty. Their mean age was 68 years. The cohort was 76% men, 34% white, 34% black, 23% Hispanic, and 9% other races or ethnicities. The mean body mass index was 34 kg/m², and their mean HbA1c level was 6.6% (range 4.9%-12.3%).

A multivariate analysis looking at associations between HbA1c levels and wound complications showed that higher HbA1c levels were significantly associated with a higher risk for any complications, and surgical site and wound complications after surgery.

Only four surgical site infections occurred—too few to demonstrate a specific association between HbA1c levels and wound infection—but “it is notable that three of four infections occurred in patients with an HbA1c [level] above 7.5%,” Dr. Blum said, adding that although too few complications occurred to show a significant association with HbA1c levels, an association might be seen in a larger study.

The current study found no association between HbA1c level and the risk of non-surgical-site infections, urinary retention, or discharge after surgery to an inpatient facility. Overall, 43% of the patients developed medical or surgical complications.

Future studies with [more] patients may help determine a cut-off HbA1c level above which total hip [or knee] arthroplasty can be considered too high risk,” Dr. Blum said. A 2003 review by other investigators of 286 orthopedic patients between non-cardiac surgeries found that those with an HbA1c level above 7% had a statistically significant increased risk for postoperative complications. But there have been few studies to date on the results of total knee arthroplasty in diabetes patients, and even fewer studies on the results of total hip arthroplasty in diabetes patients, he noted. Some reports suggest a risk of death for deep infection in diabetes patients after total knee arthroplasty, and overall wound complication rates of 1%-12%.

A 1983 study of outrace cases of total hip arthroplasty in diabetes patients reported superficial infections in 10% of the patients and deep infections in 7%.