

Islet Transplantation Restores Glycemic Stability

BY MARY ANN MOON
Contributing Writer

Islet transplantation using the Edmonton protocol restored long-term insulin production and glycemic stability in an international trial of 36 subjects with severe type 1 diabetes. However, the insulin independence that many of them initially achieved usually was not sustainable.

Nevertheless, even residual islet function without insulin independence still produced marked glycemic control and full protection from severe hypoglycemic episodes.

These results demonstrate that the Edmonton protocol for islet preparation and posttransplantation care is feasible and can be reproduced, although "normal endocrine reserve is rarely achieved, and insulin independence is gradually lost in most cases over time," reported Dr. A.M. James Shapiro of the University of Alberta, Edmonton, and his associates.

The results demonstrate that the Edmonton protocol for islet preparation and post-transplantation care is feasible and can be reproduced.

The trial was conducted at six North American and three European medical centers. Each site followed four patients with diabetes of at least 5 years' duration who had failed on optimal insulin therapy with intensive glycemic monitoring. The subjects received up to three islet infusions and were followed for a mean of 41 months.

At 1 year post transplant, 16 of the 36 subjects (44%) had achieved glycemic control independent of insulin therapy, Dr. Shapiro and his associates said (N. Engl. J. Med. 2006;355:1318-30).

Another 10 subjects (28%) showed partial graft function, achieving complete protection from severe hypoglycemia and markedly improved glycemic control.

The remaining 10 subjects had complete graft loss and did not show clinical improvement. The graft never functioned in four of them and failed early in another two; the remaining four patients withdrew from treatment.

At 2-year follow-up, islet cell function had declined so that only 5 of the 16 subjects who had initially achieved insulin independence still retained it. The reason for this

gradual loss is unknown, but one possible explanation is "metabolic exhaustion from chronic overstimulation of a marginal islet engraftment mass," the investigators said.

There were 23 serious adverse events related to treatment, including reactions to immunosuppression in five patients and acute intraperitoneal bleeding from the procedure in seven. A "worrisome" decline in renal function was noted in some and was attributed to the combined toxic effects of immunosuppressive drugs on

preexisting diabetic nephropathy.

"Islet transplantation may best be considered as an evolving therapy for use in highly selected patients with severe hypoglycemia or labile type 1 diabetes mellitus, provided all other attempts to stabilize glycemic control have been exhausted. For patients seeking long-term independence from insulin, whole-pancreas transplantation appears to offer more robust metabolic reserve at the present time," they added.

In an editorial comment accompanying

this report, Dr. Jonathan S. Bromberg and Dr. Derek LeRoith of the Mount Sinai School of Medicine, New York, said that the Edmonton protocol "is clearly orders of magnitude better than previous attempts at islet transplantation."

However, the poor long-term results, high cost, and relatively high rate of major and minor adverse events "make it difficult to argue for expansion of islet transplantation to the general population," they said (N. Engl. J. Med. 2006;355:1372-4). ■

Give your patients the convenience of **one**

One insulin. Two actions.
One simple way to help control diabetes.

NovoLog® Mix 70/30 is...

- **Complete coverage**—for both FPG and PPG^{1,2}
- **Effective**—QD, BID, and TID dosing gets up to 77% of patients to ADA goal^{3*}
- **Easy**—no carb counting required
- **Safe**—low rate of hypoglycemia^{4,5}
- **The patient-preferred pen[†]**—NovoLog® Mix 70/30 FlexPen^{®6}
- **Covered**—on most managed care formularies

NovoLog® Mix 70/30 meets AACE-recommended guidelines for patients new to insulin with A1C >8.5%.⁷

Satisfaction Guarantee[‡] to help patients progress toward glycemic goals.

*ADA goal is A1C <7%.

[†]74% of patients preferred NovoLog® Mix 70/30 FlexPen versus 9% who preferred insulin lispro mix 75/25 prefilled pen for overall ease of use. 17% of respondents had no preference.

[‡]Subject to program details included in the Satisfaction Guarantee Patient Folio.

A1C targets achieved with NovoLog® Mix 70/30³

NovoLog® Mix 70/30 dosing schedule	A1C <7% (ADA goal)	A1C ≤6.5% (AACE, IDF goal)
QD (dinner)	41%*	21%*
BID (breakfast, dinner)	70%*	52%*
TID (breakfast, lunch, dinner)	77%*	60%*
Total ITT (intent-to-treat) population	77/100	60/100

*Cumulative percent of patients achieving A1C goals.

48-week, open-label, observational study in 100 patients 18 years and older with type 2 diabetes for ≥12 months and A1C levels between 7.5% and 10%. Patients had been previously treated on stable antidiabetic regimen for at least 3 months. NovoLog® Mix 70/30 was initiated once daily during phase 1 and titrated in phases to dosing schedules of BID (phase 2) and TID (phase 3) as needed to reach treatment goals. Subjects achieving an A1C level of ≤6.5% were considered to have completed the study. Patients not achieving A1C ≤6.5% continued to phases 2 and 3.³

NovoLog® Mix 70/30
70% insulin aspart protamine suspension and
30% insulin aspart injection, (rDNA origin)

Give your patients the simplicity of **one**

Important Safety Information: Because NovoLog Mix 70/30 has peak pharmacodynamic activity 1 hour after injection, it should be administered with meals. Any change of insulin should be made cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, species, or method of manufacture may result in the need for a change in dosage. NovoLog Mix 70/30 is contraindicated during episodes of hypoglycemia and in patients hypersensitive to NovoLog Mix 70/30 or one of its excipients. Because of differences in the action of NovoLog Mix 70/30 and other insulins, care should be taken in patients in whom these conditions may be clinically relevant (eg, patients who are fasting, have autonomic neuropathy, are using potassium-lowering drugs, or are taking drugs sensitive to serum potassium level). Do not mix NovoLog Mix 70/30 with any other insulin product.

The significance, with respect to the long-term clinical sequelae of diabetes, of the differences in postprandial hyperglycemia between treatment groups has not been established.

Indications and Usage: NovoLog Mix 70/30 is indicated for the treatment of patients with diabetes mellitus for the control of hyperglycemia.

Please see brief summary of Prescribing Information on next page.

FlexPen and NovoLog are registered trademarks of Novo Nordisk A/S.
© 2006 Novo Nordisk Inc. 129959 January 2006

Explaining Common Health Care Terms

Brochures explaining the common terms used in the diagnosis and treatment of breast cancer, heart disease, and diabetes are available to help patients better understand their conditions. For more information, and to obtain sample copies of the brochures, contact the Medical Library Association by sending an e-mail to info@mlahq.org. ■

