Islet Transplantation Restores Glycemic Stability

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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.

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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). ■

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. ■