

Studies test new approaches to islet transplantation

Researchers from 11 medical centers in the United States, Canada, Sweden, and Norway have begun testing new approaches to transplanting clusters of insulin-producing islets in adults with difficult-to-control type 1 diabetes. The clinical studies, funded by the National Institutes of Health (NIH), will determine whether changes to current methods of islet transplantation lead to improved, long-lasting control of blood glucose with fewer side effects.

In islet transplantation, clusters of islets are extracted from a donor pancreas and infused into the recipient's liver. In a successful transplant, the islets become embedded in the liver and begin producing insulin.

“A major goal of the NIH research program in type 1 diabetes is to develop therapies that replace the insulin-producing cells destroyed by the autoimmune process,” said NIH Director Elias A. Zerhouni, M.D. “These studies, which build on advances in immunology and transplantation research, may open the door to more widespread use of islet transplantation for patients with severe type 1 diabetes.”

About 5 percent to 10 percent of the nearly 21 million people with diabetes have type 1, formerly known as juvenile onset diabetes or insulin-dependent diabetes. In type 1 diabetes, a person's own immune cells attack and destroy pancreatic beta cells, which produce the hormone insulin needed for survival. Beta cells, along with several other types of cells that work together to balance blood glucose, reside in islets, also known as islets of Langerhans, in the pancreas. Three or more insulin injections a day or treatment with an insulin pump are often needed to maintain blood glucose control, but most people with type 1 diabetes still develop complications, including damage to the heart and blood vessels, eyes, nerves, and kidneys. Despite steady improvements in managing the disease, type 1 diabetes cuts lives short by about 15 years, with early deaths due mainly to heart attacks and strokes.

In 2000, a research team led by Dr. James Shapiro at the University of Alberta in Edmonton, Canada, reported sustained insulin independence in seven patients transplanted with islets from two to four donor pancreases and treated with an immunosuppressive regimen that omitted glucocorticoids, thought to be toxic to islets. In the next few years, other researchers replicated the “Edmonton protocol,” and most centers adopted this approach to islet transplantation.

The protocol greatly benefits some patients with severe type 1 diabetes, but two or more infusions of islets are usually needed, and the islets tend to lose their insulin-producing function over time. Participating in an islet transplant study is appropriate for people with severe hypoglycemia (dangerously low levels of blood sugar) and for those with type 1 diabetes who have had a kidney transplant to treat kidney failure, a complication of diabetes.

Since the Edmonton advance, scientists have been working to lengthen the survival of donor islets and reduce the side effects--such as anemia, nerve and kidney damage, and vulnerability to infection--of drugs that prevent the body's destruction of donor islets. In the new studies, the researchers will culture islets before transplantation to enhance their viability. They will also compare specific anti-rejection drugs for the ability to maximize islet survival while reducing toxicity. As the procedure becomes safer and new sources of beta cells become available, more people are likely to benefit.

The researchers are conducting pilot, or phase 1/2, studies of experimental agents as well as phase 3 studies that modify the Edmonton protocol. If the phase 3 studies succeed in safely controlling blood glucose

levels, the investigators may ask the Food and Drug Administration to approve the procedure for people with poorly controlled type 1 diabetes. (For information about the phases of clinical trials, see http://www.fda.gov/fdac/features/2003/503_trial.html.)

“If these approaches are successful in prolonging islet function with less drug toxicity, type 1 diabetes patients with severe problems controlling their blood glucose may have another treatment option for controlling their diabetes,” said study chair Dr. Camillo Ricordi of the University of Miami.

The studies are enrolling individuals with type 1 diabetes who have serious difficulty controlling their blood glucose despite intensive medical therapy and who suffer from episodes of severe hypoglycemia (dangerously low levels of blood glucose). Also eligible are patients with severe hypoglycemia and hypoglycemia unawareness, who cannot sense a drop in blood glucose and may lose consciousness without warning. In addition, researchers are accepting type 1 diabetes patients who have had a kidney transplant and are already taking immunosuppressive drugs.

Source: National Institute of Diabetes and Digestive and Kidney Diseases

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