Medical Xpress

Islet transplantation improves QoL for people with hard-to-control type 1 diabetes

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Quality of life for people with type 1 diabetes who had frequent severe hypoglycemia—a potentially fatal low blood glucose (blood sugar) level—improved consistently and dramatically following transplantation of insulin-producing pancreatic islets, according to findings published online March 21 in *Diabetes Care*. The results come from a Phase 3 clinical trial funded by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), both part of the National Institutes of Health.

The greatest improvements were seen in diabetes-related quality of life. Islet recipients also reported better overall health status after transplant, despite the need for lifelong treatment with immune-suppressing drugs to prevent transplant rejection. Researchers observed these improvements even among transplant recipients who still required insulin therapy to manage their diabetes.

The trial enrolled 48 people with type 1 diabetes who had hypoglycemia unawareness—an impaired ability to sense drops in blood glucose levels—and experienced frequent episodes of severe hypoglycemia despite receiving expert care.

Previously reported clinical outcomes from the trial showed that islet transplantation prevents severe hypoglycemia and improves blood glucose awareness and control. The study was conducted by the NIH-funded Clinical Islet Transplantation Consortium.

"Although insulin therapy is life-saving, type 1 diabetes remains an extremely challenging condition to manage," said NIAID Director Anthony S. Fauci, M.D. "For people unable to safely control type 1 diabetes despite optimal medical management, islet transplantation offers hope for improving not only physical health but also overall quality of life."

Pancreatic islets release the hormone insulin, which helps control blood glucose levels. In type 1 diabetes, the body's immune system attacks and destroys the insulin-producing cells in islets. People with the disease must take insulin to live, but insulin injections or pumps cannot control blood glucose levels as precisely as insulin released naturally from the pancreas. Even with diligent monitoring, blood glucose can often reach levels that are higher or lower than normal.

A low blood glucose level, or hypoglycemia, typically is accompanied by tremors, sweating, nausea and/or heart palpitations. These symptoms prompt the person to eat or drink to raise their blood glucose. However, some people do not experience these early warning signs. This impaired awareness of hypoglycemia raises the risk of potentially life-threatening severe hypoglycemic events, during which the person is unable to treat himself or herself. These episodes can lead to accidents, injuries, coma and death.

"People with type 1 diabetes who are at high risk for hypoglycemic events have to practice caution every moment, even while sleeping. It is an exhausting endeavor that—like the events themselves—can keep them from living full lives," said NIDDK Director Griffin P. Rodgers, M.D. "Although islet transplantation remains experimental, we are very encouraged by these findings, as we are by the rapid improvements in other treatments to help people with type 1 diabetes monitor and manage their blood glucose, including artificial pancreas technology."

All 48 study participants received at least one islet transplant. One year after their first transplant, 42 participants (88 percent) were free of severe hypoglycemic events, had established near-normal blood glucose control, and had restored awareness of hypoglycemia. Only a small number of functional insulin-producing cells are necessary to restore hypoglycemic awareness, but this amount may not be sufficient to fully regulate a person's blood glucose levels. Approximately half of the transplant recipients needed to continue taking insulin to control their blood glucose levels.

The study design incorporated four well-established, commercially available quality-of-life surveys that were given to participants repeatedly before and after islet transplantation. Two of the surveys were specific for diabetes, while two assessed health more generally.

"This study was very rigorous both in terms of the number of measures used to assess quality of life and the number of evaluations performed," said paper co-author Nancy D. Bridges, M.D., chief of the Transplantation Branch at NIAID. "Islet transplant recipients not only reported a decrease in concerns and fears related to their diabetes, but also felt better overall, despite the need to take daily immunosuppressive drugs to prevent transplant rejection."

Reported improvements in quality of life were similar among islet recipients who still needed to take insulin to manage their diabetes and those who did not. The researchers concluded that elimination of severe hypoglycemia and the associated fears accounted for these improvements, appearing to outweigh concerns about the need to continue insulin injections.

Islet transplantation is an investigational therapy in the United States. While promising for people whose type 1 diabetes cannot be controlled with standard treatments, the procedure is not appropriate for most

people with type 1 diabetes, as there are risks associated with the transplant procedure, such as bleeding, as well as side effects of immunosuppressive medications, such as decreased kidney function and increased susceptibility to infections.

In the NIH-funded trial, investigators at eight study sites in North America used a standardized manufacturing protocol to prepare purified islets from the pancreases of deceased human donors. The study was designed, after discussions with the U.S. Food and Drug Administration, to provide evidence to support licensure of the manufactured islet product. NIAID, the regulatory sponsor of the study, has submitted final reports and clinical trial data to FDA, laying the groundwork for individual universities and companies to submit biologics license applications for the manufacture of purified human pancreatic islets.

More information: Eric D. Foster et al, Improved Health-Related Quality of Life in a Phase 3 Islet Transplantation Trial in Type 1 Diabetes Complicated by Severe Hypoglycemia, *Diabetes Care* (2018). DOI: 10.2337/dc17-1779

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