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Title **Islet Transplantation for the Treatment of Type 1 Diabetes – An Update**

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Aim

To evaluate the safety and efficacy/effectiveness of islet transplantation alone (ITA) in comparison with intensive insulin therapy, or whole organ pancreas transplantation for patients with nonuremic type 1 diabetes with severe hypoglycemia or hypoglycemia unawareness.

Conclusions and results

Fourteen primary studies met the inclusion criteria. None of the studies reported any ITA-related deaths. Procedure-related complications, eg, intraperitoneal bleeding and portal vein thrombosis, occurred in up to 25% and 17% of patients, respectively. Most patients had elevated liver enzyme levels, which returned to normal within 1 month of transplantation. Up to 50% of patients showed immunosuppression-related decline in renal function.

Limited evidence from 11 case series studies (n=208 patients) showed that transplanting an adequate mass of islet cells (from 2 to 3 pancreas donors) restored insulin independence in the short term (≤1 year), achieving adequate glycemic control in 30% to 69% of patients. However, islet function deteriorated over time. Only 14% of patients remained insulin-independent at 2 years in one multicenter study. In another study, fewer than 10% of patients remained insulin-free at 5 years.

Two studies (n=109 patients) reported inconsistent results for overall health-related quality-of-life measures. Results from two poorly designed studies (n=22 patients) showed improvement in diabetic retinopathy and neuropathy 1 year after ITA.

None of the primary research studies compared ITA with intensive insulin therapy, or whole organ pancreas transplantation alone in nonuremic patients with severe hypoglycemia or hypoglycemia unawareness.

Recommendations

ITA may be relatively safe and effective in the small group of nonuremic type 1 diabetic patients with severe hypoglycemia and uncontrolled diabetes, and for whom the benefits of stable glycemia and freedom from hypoglycemia outweigh the potential risks of islet transplantation. However, it is premature to consider ITA as 'standard care'. ITA faces major obstacles, eg, lack of a readily available source of human islets and the need for chronic immunosuppressive therapy.

Methods

All relevant full-text systematic reviews, health technology assessments (HTA), and primary studies, published in English, were identified by systematically searching the Cochrane Library, the Centre for Reviews and Dissemination databases (NHS EED, HTA, DARE), PubMed, EMBASE, CINAHL, the Web of Science, and the websites of various HTA agencies, research registers, evidence-based resources, and practice guideline clearinghouses from Nov 2002 to May 2008. Two reviewers independently assessed the methodological quality of the included studies.

Further research/reviews required

For islet transplantation to be a potential long-term (>1 year) treatment option, further research is needed to: improve the sensitivity of methods to detect graft loss; find ways to preserve islet mass over time; reduce the number of islets required to reverse diabetes; and decrease the toxicity of immunosuppressive regimens. Studies with longer follow-up (>5 years) need to track the durability of patient outcomes and examine the effect of ITA on secondary complications of diabetes. Quality-of-life tools specific for ITA patients are required to quantitatively record patient outcomes.

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