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Pancreatic islet transplantation: A promising treatment for "brittle" type 1 diabetes

Transplantation of islets isolated from deceased donor pancreas (ITA) is a promising minimally invasive treatment for patients suffering from severe form of type 1 diabetes to attain normoglycemia. Although this treatment was conceptualized more than a century ago, its application in clinical practice has seen a remarkable increase only from the year 2000. It is the only procedure known to provide a "transient cure" for type 1 diabetic patients in terms of their dependence on exogenous insulin use. Despite offering several advantages as a treatment for autoimmune diabetes, ITA is also facing several hurdles in its broader implementation. The quality of donor pancreas, islet isolation methodology, islet engraftment and immunosuppression play major role in the success of clinical islet transplants. A unique innate immune response against intraportally transplanted islets called instant blood-mediated inflammatory reaction causes significant destruction (~50% of transplanted islet mass) affecting the islet engraftment. According to the recent report by the collaborative islet transplant registry, 864 type 1 diabetic patients have received 1679 islet transplants. It is common for one patient to receive more than one islet transplant to achieve an optimal islet dose. The clinical outcomes have demonstrated that ITA is highly efficient in the prevention of severe hypoglycemic events. In terms of attainment of insulin independence, ITA has shown remarkable progress in recent years with ~50% of the recipients retaining the insulin independent status at 5 years post-transplant. Introduction of polyclonal T cell depleting antibodies and anti-inflammatory drugs during induction period were the major reasons for the improvement in islet graft function. A recently completed phase III clinical trial has confirmed the safety and efficacy of ITA. Our team has introduced a combination of Etanercept and Anakinra, which block TNF-α and IL-1β respectively, in a cohort of islet transplant patients and have shown improved islet graft function. Effective control of alloimmune and autoimmune responses may significantly improve the islet graft function. Increased clinical application of ITA is also awaiting approval of biological license application by the Food and Drug Administration.

Biography

Bashoo Naziruddin has been the Director of the cGMP Islet Cell Processing Laboratory at Baylor University Medical Center since April 2003. He is also an Adjunct Associate Professor at the Institute of Biomedical Studies at Baylor University, Waco, Texas. His current research is focused on "Immunobiology of human islet cell transplantation". His specific research topics include assessment of immune response in islet transplant recipients, development of an optimal immunosuppressive regimen for islet transplantation, strategies to induce tolerance towards donor islets, identification of novel drugs to prevent islet rejection, and potential use of islets from pigs for transplantation into humans. He has published more than 113 research articles in peer-reviewed journals and has co-authored chapters in two books on Organ Transplantation and Type 1 Diabetes. He has also given more than 126 presentations at international/national scientific meetings and has delivered invited talks at reputed institutions.

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