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Advancements and Challenges in Islet Transplantation

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Islet transplantation is an established therapeutic procedure in which islets isolated from pancreas of cadaveric organ donors are transplanted into the portal vein of a subset of type 1 diabetic patients with complicated glycemic control. Over the last eight years, more than 850 islet transplants have been performed in more than 30 international transplant centers according to the International Islet Transplant Registry. Islet transplantation is being performed by normothermic perfusion, a minimally invasive procedure with fewer potential complications than full pancreas transplantation [1]. Clinical islet transplantation achieves insulin independence for up to 5 years post-transplant and provides patients with a stable glycemic control and a reduction of hypoglycemic events. Further, patients that have been transplanted and are back on insulin remain c-peptide positive and present an amelioration of glycated hemoglobin and a decrease in the progression of vascular complications [2].

Though clinical success has improved markedly over the past years, several obstacles must be overcome for a widespread implementation in the diabetic population. Such challenges can be included in three main categories: a shortage of donor tissue, the need for immunosuppressive therapy, and the improvement of the short- and long-term function and viability of islets in grafts. First, a shortage of donor tissue can be overcome by the optimization of islet isolation methods to achieve single-donor transplant (current islet transplant recipients receive islets from an average of 2-3 donors) [3]. The routine implementation of these novel isolation methods will reduce the risk of donor HLA sensitization, will decrease the number of donors, and subsequently, will increase the number of patients to be treated [3,4]. On the other hand, novel strategies such as the use of islets from other animal sources (for example, pigs) [5], stem cell differentiation [6], gene therapy [7] or engineered beta cell lines [8] could be made to work successfully if they reach the stage of clinical applicability. Second, immunosuppressive or anti-rejection drugs are needed to keep the transplanted islet grafts functioning and an effective control of both alloimmune and autoimmune attack is crucial for the success of the treatment. Nevertheless, current immunosuppressive drugs, such as tacrolimus and sirolimus are known to be toxic to β-cells and may have detrimental effects in β-cell function [9]. Thus, improvement of immunosuppressive and anti-rejection drugs and regiments would benefit the transplant outcome. Though, the ultimate goal of islet transplantation is to prevent the use of immunosuppressive treatment, making the use of strategies to promote donor-specific tolerance in recipients a critical research area in the future [7,10]. Finally, islet grafts in the hepatic microenvironment fail slowly and progressively despite aggressive immunosuppressive therapy, probably as a result of the low levels of oxygen, increased amyloid deposition and the continuous inflammatory milieu before undergoing revascularization [11,12]. This encompasses a loss of graft function during the post-transplantation period. To overcome this problem researchers are investigating the use of additional alternative sites, such as muscle or other organs [13,14]. These studies should continue to optimize islet engraftment and function in the transplantation environment.

In conclusion, the impact of islet transplantation in type 1 diabetic recipients is crucial and alternative and novel methods are being discovered to improve graft outcome. Future studies will no doubt improve islet transplantation success and further open this treatment to all diabetic population.

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